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Consistent Pattern of Elevated Symptoms in Air-conditioned Office Buildings: A Reanalysis of Epidemiologic Studies

MARK J. MENDELL, MPH, AND ALLAN H. SMITH, MD, PHD

Abstract: Published studies of the relation between type of building ventilation system and work-related symptom prevalence in office workers have been contradictory. A reanalysis was performed of six studies meeting specific eligibility criteria, combining published data with unpublished information obtained from study authors. Five eligible studies were from the United Kingdom, and one was from Denmark. Standardized categories of building ventilation type were created to allow comparison of effects across studies. Within each study, prevalence odds ratios (PORs) were calculated for symptoms in each ventilation category relative to a baseline category of naturally ventilated buildings. Air-conditioned buildings were consistently associated with increased prevalence of work-related headache (POR = 1.3-3.1), lethargy (POR = 1.4-5.1), and upper respiratory/mucus membrane symptoms (POR = 1.3-4.8). Humidification was not a necessary factor for the higher symptom prevalence associated with air-conditioning. Mechanical ventilation without air-conditioning was not associated with higher symptom prevalence. The consistent associations found between type of building ventilation and reported symptom prevalence have potentially important public health and economic implications. (*Am J Public Health* 1990; 80:1193–1199.)

Introduction

Health problems and non-specific symptom complaints apparently related to buildings or indoor air, sometimes referred to as "sick building syndrome" or "tight building syndrome," have been recognized for over 15 years[1]. Although particular chemical,[2] biological,[3] physical,[4] or psychological[5] factors have been implicated in some episodes, specific causes have generally not been identified.[6] Studies of this problem to date, generally carried out in buildings identified by worker complaints (referred to herein as "complaint" buildings) have demonstrated mostly what these episodes are *not*. They are not caused by known toxins at concentrations exceeding current health standards nor are they generally associated with known diseases. We still have little idea how frequently the excess symptoms reported in such episodes actually occur among office workers, or what if any chronic health problems in this population are related to office buildings.

It is difficult to study a phenomenon characterized only by self-reported non-specific symptoms with no accepted syndrome definition or objective tests available. A major weakness of investigations in buildings with widely recognized worker complaints is that occupant concerns are likely to upwardly bias symptom reporting, thus distorting the only outcome available for study. Until the development of useful objective tests, it will therefore be preferable to study buildings without recognized worker complaints (referred to herein as "non-complaint" buildings).

Reports on building-related health problems in the United States are almost without exception case studies of complaint buildings;[2–4,7–10] only one study compared the building under investigation to even a single noncomplaint building.[11] A number of recent European studies, however, have provided data from non-complaint buildings on relations between work-related symptoms in office workers and type of building ventilation.[12–16] Preliminary review of the European studies shows that mechanical ventilation, relative to natural ventilation, has been associated with increases,[12,16] with decreases,[17] and with no differences[22] in work-related symptoms; air-conditioning, has been associated with increases[17] and with no differences[16] in symptoms. Previous reviews of the literature on illness episodes in office buildings[6,27–30] have summarized available studies but have not discussed these discrepancies.

This paper presents a reanalysis of data from non-complaint building studies. The purpose was to determine if there were consistent relations between prevalence of specific symptoms and certain building ventilation factors: mechanical ventilation, air conditioning, and humidification. Although differences between the original studies did not allow direct comparison of results, additional information obtained from study authors allowed creation of a standardized set of ventilation categories, calculation of prevalence odds ratios, and comparison of findings across studies.

Methods

Selection of Studies for Reanalysis

Studies of work-related symptoms in office workers were selected from the literature, using specific eligibility criteria. For inclusion in this reanalysis it was required that:

- studies compared multiple non-complaint office buildings;
- data allowed comparison of prevalence for specific work-related symptoms between buildings of different ventilation type; and
- data were available allowing classification of buildings as naturally or mechanically ventilated, as air-conditioned or not air-conditioned, and as humidified or not humidified.

Six studies of worker symptoms in multiple office buildings[12–26] were included in this reanalysis. The studies included were all cross-sectional and compared work-related symptom prevalence in buildings with different ventilation types to a baseline symptom prevalence in naturally ventilated buildings. All studies tested for statistical independence of ventilation categories and symptom prevalence (using chi square or analysis of variance tests) but used no epidemio-

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From the Department of Biomedical and Environmental Health Sciences, University of California, Berkeley (both authors) and the California Department of Health Services (Mendell). Address reprint requests to Mark J. Mendell, MPH, Environmental Epidemiology and Toxicology Section, California Department of Health Services, 5900 Hollis Street, Suite E, Emeryville, CA 94608. This paper, submitted to the Journal November 3, 1989, was revised and accepted for publication April 9, 1990.

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logic effect measures (such as prevalence ratios or odds ratios) to assess this relationship. Five studies were conducted in the United Kingdom, and one in Denmark. (Findings of the six studies are summarized in the Appendix.)

Methods of Analysis

Five standard categories of building ventilation type were established, as described in Table 1. Information for this classification was extracted from published materials; where necessary, additional information was obtained directly from the authors, and subsequent classification of buildings was confirmed with them.* Ultimately, sufficient information was available for unequivocal classification of all buildings from the six studies into this common set of categories. Correct conversion of ventilation categories in the original studies to the ventilation categories in this reanalysis was not always straightforward; in such cases, the appropriate conversions are provided in footnotes to Table 2, along with publications from which the data were obtained.

Symptoms were organized into four groups:

- lower respiratory (tight chest, difficulty breathing, shortness of breath, wheeze, and flu-like symptoms);
- upper respiratory/mucus membrane (nose, throat, and eye symptoms);
- central nervous system (headache and lethargy); and
- skin (dry skin, itching skin, and skin rash).

From sample size and prevalence data reported for either individual buildings or groups of buildings in each study, numbers of subjects with and without each specific work-related symptom were calculated within each category of building ventilation type. Prevalence rates were then calculated. "Work-related symptoms" in all studies referred only to symptoms reported as improving on weekends or days away from work (and in study 1 and parts of study 2, also as having begun or worsened since starting work in the current building). Symptom frequency requirements varied between studies.

Baseline symptom prevalence varied widely between studies. Using the naturally ventilated building category as the reference group within each study, prevalence odds ratios and 95% test-based confidence limits[31] were calculated from prevalence rates for each work-related symptom within each of the other ventilation categories. The prevalence odds ratio was chosen as the most informative epidemiologic effect measure for cross-sectional prevalence data.[32,33]

Results

Table 2 gives the sample sizes for each study reviewed, in terms of number of workers and number of buildings in each ventilation category.

Table 3 gives prevalence data for specific work-related symptoms, as calculated for each study using the new building ventilation categories.

Table 4 gives prevalence odds ratios (PORs) for each work-related symptom in each ventilation category. Symptom prevalence in category II buildings (with simple mechanical ventilation) was comparable to that in category I buildings or lower, with one exception (headache prevalence in study 4, based on only one building in category II). This was in sharp contrast to the general pattern of higher symptom prevalence in air-conditioned buildings (categories III, IV, and V) found in all six studies.

The prevalence of central nervous system and upper respiratory/mucus membrane symptoms was almost without exception higher in the air-conditioned buildings than in the naturally ventilated buildings. Data on lower respiratory problems were relatively sparse and less consistent. Data on skin-related symptoms suggested higher prevalence in air-conditioned buildings.

Data on differences between air-conditioned buildings with different kinds of humidification were mixed. In studies 1 and 3, where these data were available, symptom prevalence in buildings with steam humidification was similar to that in those with no humidification. There was some suggestion in both studies of higher symptom prevalence in buildings with water-based humidification relative to both categories III and IV. For 18 of the 21 symptoms assessed between these two studies, point estimates in category V equaled or exceeded those in both categories III and IV.

In study 2, on the other hand, symptom prevalence in air-conditioned buildings with water-based humidification was generally comparable to or lower than that in air-conditioned buildings without humidification. More complete data from this study, however, were presented at a scientific meeting. They showed consistently *lower* symptom prevalence in air-conditioned buildings with water-based humidification than in those without humidification; symptom prev-

TABLE 1—Building Ventilation Categories for Comparison Across Studies

	Building Ventilation Categories				
	I	II	III	IV	V
Ventilation Characteristics	Natural*	Simple Mechanical**	Air-Conditioned No Humidification	Air-Conditioned Steam Humidification	Air-Conditioned Water-Based Humidification
Mechanical ventilation	No	Yes	Yes	Yes	Yes
Air-conditioning	No	No	Yes	Yes	Yes
Steam humidification	No	No	No	Yes	No
Drip, spray, or evaporative humidification	No	No	No	No	Yes

*operable windows only
**ducted airflow without cooling or chilling

---

*Personal communications: M. Finnegan, S. Burge, A. Pickering, A. Robertson, J. Harrison, O. Valbjorn.

TABLE 2—Study Sample Sizes by Building Ventilation Category

Study	Sampling Unit (Total N)	Building Ventilation Categories I Natural[*] (N)	 II Simple Mechanical[**] (N)	 III Air-Conditioned No Humidification (N)	 IV Air-Conditioned Steam Humidification (N)	 V Air-Conditioned Water-Based Humidification (N)
1[*]	Workers (951)	259	—	73	91	528
	Buildings (8)	3	—	1	1	3
2[**]	Workers (2587)	537	—	507	—	1543
	Buildings (27)	8	—	6	—	13
3[***]	Workers (4373)	442	944	1017	421	1549
	Buildings (47)	11	7	10	4	15
4[†]	Workers (1332)	206	118	—	—	1008
	Buildings (5)	2	1	—	—	2
5[††]	Workers (106)	47	—	—	—	59
	Buildings (2)	1	—	—	—	1
6[†††]	Workers (2778)	1166	1430	—	—	182
	Buildings (14)	6	7	—	—	1

[*] Source: Reference 15 was used, as it included an additional, steam-humidified, building not included in the initial report, reference 12, and it omitted two buildings included in the initial report specifically because of worker complaints. Category III buildings were described as having "mechanical ventilation."

[**] Source: Reference 16. Category III buildings were described as having "mechanical ventilation only." Category V buildings were described as "fully air-conditioned, with or without recirculation," or "humidified."

[***] Source: Reference 17 was used for data in categories I and II, but reference 19 was used for categories III-V, as it was the only report to include data from air-conditioned buildings by type of humidification, for all symptoms.

[†] Source: Reference 20. Category I buildings were described as "conventional" and category II as "unconditioned."

[††] Source: Reference 21.

[†††] Source: Reference 22. Data used were from the 14 town halls; buildings number 10, 20, 30, 40, 50, and 90 were in category I, number 121 was in category V, and the rest were in category II.

alence was still substantially higher than in naturally ventilated buildings.[**]

Buildings without natural ventilation may be sealed (i.e., have non-operable windows) or not. Although sufficient information was not available to allow incorporation of this factor into ventilation categories used for reanalysis, enough information was available to show a very strong relation between the presence of air-conditioning and presence of sealed windows in the buildings studied: only one of the 48 non-air-conditioned buildings had sealed windows, whereas 52 of the 57 air-conditioned buildings had sealed windows. Thus, given the limits of these data, symptom increases found to be associated with air-conditioned buildings may more appropriately be regarded as associated with air-conditioned, sealed buildings.

Discussion

This reanalysis suggests that sealed buildings with air-conditioning are associated with higher prevalence of work-related headache, lethargy, and eye, nose, and throat symptoms than unsealed buildings with no air-conditioning, even in the absence of humidification. It also suggests that although air-conditioned buildings with steam humidification are associated with symptom prevalence no higher than air-conditioned buildings without humidification, air-conditioned buildings with water-based humidification *may* be associated with higher prevalence of eye, nose, and throat symptoms than those with steam humidification.

Apparent discrepancies between the original reports were resolved by reclassification based on new information from authors of the studies. Buildings described as mechanically ventilated were actually air-conditioned without humidification in studies 1 and 2, and simply mechanically ventilated in study 3; in study 6, they were simply mechanically ventilated or, in one case, air-conditioned with water-based humidification.

The prevalence of some work-related symptoms was strikingly high in several studies in even the least problematic office buildings, suggesting a measurement problem. High prevalence of lethargy in category I buildings in studies 3 and 5 (50 percent and 62 percent) in fact reflects a very broad definition of "work-related" symptoms in these two studies, the least restrictive such definition in all studies reviewed (see Appendix). (That such high prevalence resulted from specifics of the study protocol is evident from the fact that study 5 remeasured buildings from study 1 with the protocol from study 3, and obtained prevalence estimates two to four times those in study 1, comparable to those in study 3.)[21] Symptom prevalences reported in study 6, also somewhat high, represented combinations of two to three specific symptoms assessed.[10] Such differences emphasize the need for standardized questionnaire design and data reporting.

One must be cautious in generalizing results of this reanalysis. The studies reviewed were all carried out in the United Kingdom or Denmark, and other countries may have differences in climate as well as in building and ventilation system design or operation.

Also, limitations in the data restrict conclusions that can be drawn from this reanalysis, due to a variety of possible biases in each study.

Bias from selection of buildings seems unlikely, as buildings in all studies were selected independently of worker complaints. Response bias among workers also seems unlikely, as response rates were high in all studies (see Appendix). Some selection bias due to cross-sectional study design

---

[**] J. Harrison, presented at Indoor Air Quality 89, San Diego, CA, April 17–20, 1989.

TABLE 3—Prevalence of Reported Work-related Symptoms among Office Workers by Building Ventilation Category

		Building Ventilation Categories				
Study	Symptoms	I Natural (%)	II Simple Mechanical (%)	III Air-Conditioned No Humidification (%)	IV Air-Conditioned Steam Humidification (%)	V Air-Conditioned Water-Based Humidification (%)
	Central Nervous System					
1	headache	15.7	—	37.0	29.7	32.0
	Lethargy	13.8	—	45.2	29.7	41.3
2	Headache	20.7	—	39.3	—	35.6
	Lethargy	19.1	—	49.9	—	43.3
3*	Headache	39	33	45	48	47
	Lethargy	50	42	58	60	65
4*	Headache	20	36	—	—	40
5*	Headache	32	—	—	—	66
	Lethargy	62	—	—	—	86
6*	Headache, fatigue, or malaise	33	35	—	—	53
	Upper Respiratory/Mucus Membrane					
1	Nose symptoms	5.8	—	13.7	15.4	19.1
	Dry throat/blocked nose	8.1	—	17.8	16.5	29.9
	Eye symptoms	5.8	—	8.2	13.2	15.9
2	Nose symptoms	13.4	—	30.7	—	22.4
	Throat symptoms	15.5	—	31.6	—	30.8
	Eye symptoms	11.0	—	19.3	—	23.1
3*	Runny nose	19	16	24	25	26
	Blocked nose	40	32	48	48	55
	Dry throat	36	33	49	47	53
	Dry eyes	18	20	31	28	33
	Itching eyes	22	20	31	27	32
4*	Sore throat, coughs, colds	21	21	—	—	44
	Irritated/sore eyes	17	20	—	—	48
6*	Eye, nose or throat symptoms	27	26	—	—	42
	Lower Respiratory					
1	Tight chest	2.3	—	1.4	1.1	6.1
	Short of breath	1.5	—	0.0	0.0	1.9
	Wheeze	3.1	—	0.0	0.0	5.1
3*	Tight Chest	6	5	10	9	12
	Difficulty breathing	6	6	10	8	12
	Flu-like symptoms	15	14	27	27	27
	Skin					
1	Dry skin	5.7	—	5.5	9.9	10.8
	Rash	1.9	—	2.7	3.3	2.1
	Itching skin	2.9	—	2.7	4.4	5.5
2	Dry skin	6.4	—	10.5	—	12.5
6*	Dry skin or rash	6	7	—	—	13

*Prevalence data originally reported as integer values.

is possible as workers who left the workplace due to illness or discomfort were not included, but this would lead to underestimation of any real effects.

Because "negative" (non-significant) studies are generally less likely to be submitted or accepted for publication, reviews of the literature are likely to contain a disproportionate number of studies with positive findings, relative to all studies actually performed on that subject.[34,35] Publication bias may in this way have inflated the magnitude of associations in this review; however, larger studies are considered less prone to this bias,[35] and PORs for air-conditioned buildings were consistently elevated even in the largest studies reviewed. Furthermore, a consistent "negative" finding of this reanalysis was not subject to such bias: symptom prevalence in simply mechanically ventilated buildings was no greater than that in naturally ventilated buildings.

Possible information biases include reporting or interviewer bias and misclassification. Reporting or interviewer bias, due to increased worker or interviewer concerns about health in sealed, air-conditioned buildings, could have increased frequency of reported symptoms in such buildings and thus led to overestimation of odds ratios. This bias cannot be ruled out.

Awareness of the research hypothesis by interviewers or subjects could have had a similar effect. Interviewers were used only in study 1, so subjects in other studies could only have inferred hypotheses from the self-administered questionnaires. In study 1, with the highest PORs of all studies reviewed, interviewers conducted most interviews without knowledge of the buildings where subjects worked, and researchers had no prior hypotheses regarding ventilation type and symptoms other than lower respiratory.[12]

Misclassification bias could have occurred from crude classification of the very complex ventilation systems found

TABLE 4—Prevalence Odds Ratios (and 95% CIs) for Reported Work-related Symptoms among Office Workers in Different Building Ventilation Categories Relative to Naturally Ventilated Buildings

		Building Ventilation Categories				
		I	II	III	IV	V
Study	Symptoms	Natural POR (95% CI)	Simple Mechanical POR (95% CI)	Air-Conditioned No Humidification POR (95% CI)	Air-Conditioned Steam Humidification POR (95% CI)	Air-Conditioned Water-Based Humidification POR (95% CI)
	Central Nervous System					
1	Headache	1.0	—	3.1 (1.7,5.7)	2.3 (1.3,4.0)	2.5 (1.6,3.8)
	Lethargy	1.0	—	5.1 (2.9,9.2)	2.6 (1.5,4.7)	4.2 (2.7,6.5)
2	Headache	1.0	—	2.5 (1.9,3.3)	—	2.1 (1.7,2.7)
	Lethargy	1.0	—	4.2 (3.2,5.5)	—	3.2 (2.6,4.0)
3	Headache	1.0	0.8 (0.6,1.0)	1.3 (1.0,1.6)	1.4 (1.1,1.9)	1.4 (1.1,1.7)
	Lethargy	1.0	0.7 (0.6,0.9)	1.4 (1.1,1.7)	1.5 (1.2,2.0)	1.9 (1.5,2.3)
4	Headache	1.0	2.2 (1.3,3.7)	—	—	2.7 (1.9,3.8)
5	Headache	1.0	—	—	—	4.2 (1.9,9.3)
	Lethargy	1.0	—	—	—	4.0 (1.6,9.9)
6	Headache, fatigue, or malaise	1.0	1.1 (0.9,1.3)	—	—	2.3 (1.7,3.1)
	Upper Respiratory/Mucus Membrane					
1	Nose Symptoms	1.0	—	2.6 (1.1,5.9)	3.0 (1.4,6.2)	3.8 (2.2,6.5)
	Dry throat/blocked nose	1.0	—	2.5 (1.2,5.1)	2.2 (1.1,4.5)	4.8 (3.1,7.6)
	Eye symptoms	1.0	—	1.5 (0.5,3.9)	2.5 (1.1,5.4)	3.1 (1.8,5.3)
2	Nose symptoms	1.0	—	2.9 (2.1,3.9)	—	1.2 (0.9,1.6)
	Throat symptoms	1.0	—	2.5 (1.9,3.4)	—	2.4 (1.9,3.1)
	Eye symptoms	1.0	—	1.9 (1.4,2.7)	—	2.4 (1.8,3.3)
3	Runny nose	1.0	0.8 (0.6,1.1)	1.3 (1.0,1.8)	1.4 (1.0,2.0)	1.5 (1.2,1.9)
	Blocked nose	1.0	0.7 (0.6,0.9)	1.4 (1.1,1.7)	1.4 (1.0,1.8)	1.8 (1.5,2.3)
	Dry throat	1.0	0.9 (0.7,1.1)	1.7 (1.4,2.1)	1.6 (1.2,2.1)	2.0 (1.6,2.5)
	Dry eyes	1.0	1.1 (0.8,1.5)	2.0 (1.5,2.7)	1.8 (1.3,2.4)	2.2 (1.7,2.9)
	Itching eyes	1.0	0.9 (0.7,1.2)	1.6 (1.2,2.1)	1.3 (1.0,1.8)	1.7 (1.3,2.1)
4	Sore throat, coughs, or colds	1.0	1.0 (0.6,1.8)	—	—	3.0 (2.1,4.2)
	Irritated/sore eyes	1.0	1.2 (0.7,2.2)	—	—	4.5 (3.2,6.5)
6	Eye, nose, or throat symptoms	1.0	1.0 (0.8,1.2)	—	—	2.0 (1.4,2.7)
	Lower Respiratory					
1	Tight chest	1.0	—	0.6 (0.1,4.8)	0.5 (0.1,3.8)	2.7 (1.2,6.4)
	Short of breath	1.0	—	0	0	1.2 (0.4,4.0)
	Wheeze	1.0	—	0	0	1.7 (0.8,3.7)
3	Tight chest	1.0	0.8 (0.5,1.3)	1.7 (1.1,2.6)	1.5 (0.9,2.5)	2.1 (1.4,3.2)
	Difficulty breathing	1.0	1.0 (0.6,1.6)	1.7 (1.1,2.6)	1.4 (0.8,2.3)	2.1 (1.4,3.2)
	Flu-like symptoms	1.0	0.9 (0.7,1.3)	2.1 (1.6,2.8)	2.1 (1.5,3.0)	2.1 (1.6,2.8)
	Skin					
1	Dry skin	1.0	—	1.0 (0.3,3.1)	1.8 (0.7,4.4)	1.8 (0.9,3.5)
	Rash	1.0	—	1.5 (0.3,8.0)	1.8 (0.4,7.9)	1.3 (0.4,4.3)
	Itching skin	1.0	—	1.0 (0.2,4.9)	1.6 (0.4,5.6)	1.9 (0.7,4.7)
2	Dry skin	1.0	—	1.7 (1.1,2.7)	—	2.1 (1.5,3.1)
6	Dry skin or rash	1.0	1.3 (0.9,1.7)	—	—	2.5 (1.6,4.1)

in large buildings. The resulting nondifferential misclassification, however, would have led to underestimation of any real effects.

A number of potential confounding factors could have affected results. Some non-building factors known to be related to symptom reporting[17,19,22]—such as particular social and work environments, gender, job types, workplace smoking, and season of measurement—could have introduced confounding if consistently associated with particular ventilation types. There is no evidence that these factors were related to building ventilation type in the buildings studied.

Studies 2, 4, and 5 reported no assessment of potential confounding factors.[16,20,21] Study 1 reported only that smoking prevalence was similar in all buildings studied.[12] For study 3, Hedge, *et al*,[19] performed a multivariate analysis examining simultaneous association of a number of factors with total number of symptoms reported by each individual. They reported that higher overall symptom prevalence was associated with air-conditioned buildings, independently of associations also found between symptom prevalence and various individual, psychological, occupational, and architectural factors.

For study 6, a multivariate analysis found that gender, job category, work activities, and psychosocial job factors were associated with work-related symptoms. Differences in symptom prevalence between buildings, however, remained substantially the same after multivariate adjustment, with symptom prevalence still highest in the single category V building.[23]

Some building-related factors may have caused confounding. Air-conditioned buildings, being on average newer than naturally or simply mechanically ventilated buildings, will be more likely to contain fluorescent lighting,[21,36] inner offices distant from windows, with no natural light,[21] "open-plan" office layouts,[20] newer synthetic materials which emit various organic compounds,[30] and materials with high absorptive surface area (such as carpets and cloth-covered partitions) capable of accumulating and re-releasing physical, chemical, or biological contaminants.[28,29,30,37] To produce spuriously the associations found, these factors would have to be strongly related to both symptom prevalence and ventilation type.[38] This possibility could not be evaluated in the studies reviewed here.

The patterns of association in this reanalysis suggest that symptom reporting is systematically related to still unidentified factors in sealed, air-conditioned buildings. If bias or confounding factors are not responsible for these patterns, these symptom increases may represent one or more as yet unidentified ventilation-related illness syndromes. Possible ventilation-related risk factors include inadequate fresh air ventilation, reduced thermal comfort, use of chemicals within ventilation systems to kill biologic agents,[27] and recirculation of infectious[39] or allergenic[30] biologic agents. Sufficient environmental data were not available from the studies reviewed to evaluate these factors (see Appendix).

Results of this reanalysis are consistent with increased exposure of workers to biologic aerosols from water within the ventilation system (i.e., on or under air-conditioning cooling coils, which dehumidify ventilation air, and in water-based humidification systems).[17,30] Inconsistent associations found between symptom prevalence and water-based humidification may reflect a dual effect of such systems: reduced risk of respiratory infections from humidification generally,[40] but increased risk of respiratory sensitization to biological contaminants (as in humidifier fever or hypersensitivity pneumonitis) from water-based humidification specifically.[41]

In conclusion, the reanalysis of epidemiologic studies presented here suggests that, at least in some countries, increases in building-related symptoms in offices may not be unusual events, but relatively common events not usually attributed to buildings. Future study of this problem, beyond investigation of complaint buildings, is advisable.

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APPENDIX

Summaries of Findings of Six Studies

Findings of the studies included in this reanalysis are summarized here; terms used to describe ventilation categories are from the studies themselves.

The first study,[12-15] involving eight buildings, found higher symptom prevalence associated with mechanical compared with natural ventilation, even higher symptom prevalence for buildings with air-conditioning, and the highest prevalence in buildings with air-conditioning and humidification. Whether air within air-conditioned buildings was recirculated did not markedly affect symptom prevalence.

The second study,[16] involving 27 buildings, reported higher symptom prevalence in both buildings with mechanical ventilation and those with air-conditioning and humidification, compared to buildings with natural ventilation. Increases in the two groups were similar. In this study, researchers included several buildings they suspected of having problems; they point out, though, that at that time the sick building syndrome was not known in the United Kingdom.*

The third and largest study,[17-19] involving 47 buildings, found lower symptom prevalence in buildings with mechanical ventilation relative to those with natural ventilation, higher prevalence in buildings with air-conditioning, and the highest prevalence in two subsets of buildings with air-conditioning: those with evaporative humidification,[18] and those with "water-based" air-conditioning systems (this refers to method of cooling the building[42,43] and is not related to type of humidification).

The fourth study,[20] involving five buildings, found prevalence of all symptoms measured to be higher in air-conditioned buildings relative to conventional (not defined in report), but prevalence of only one symptom higher in unconditioned buildings relative to conventional buildings.

The fifth study,[21] involving two buildings, found higher symptom prevalence in an air-conditioned, humidified building relative to a naturally ventilated one.

The sixth study,[22-26] involving 14 buildings (minimal data were reported on some additional buildings), found symptom prevalence in mechanically ventilated buildings higher, but not significantly so, than in naturally ventilated buildings. The oldest town halls had the lowest prevalence of symptoms.

The first two studies used physician-administered questionnaires, and defined work-related symptoms as those occurring more than twice in the previous year, and improving on days away from work;[12,16] symptoms were also required to have started or worsened since working in the current building, except for nose, throat, and eye symptoms in the second study.** All the other studies used self-administered questionnaires. Studies 3 and 5 defined work-related symptoms as those occurring more than twice in the previous year and also improving on days away from work.[17,21] Study 4 defined work-related symptoms as those reported to occur frequently at work.[20] Study 6 defined work-related symptoms as those occurring at least weekly and improving on days away from work.[22] Although individual symptoms were assessed in this study, data were reported only on groups of symptoms.

All studies achieved high response rates among workers in buildings studied—in study 1 from 75–97 percent;[12] in study 2 from 86 percent upward;[16] in study 3 from 67–100 percent, averaging 92 percent;[17] in study 5 averaging 97 percent;[21] and in study 6 from 61–93 percent, averaging 80 percent.[22]

No study reported outside air ventilation rates in buildings. In study 1, environmental measurements were taken in only two buildings, one with low and one with high symptom prevalence; no significant differences were found in the parameters measured—dry bulb temperature, globe temperature, relative humidity, air moisture content, air velocity, positive and negative ions, carbon monoxide, ozone, and formaldehyde.[14] In study 2, levels of airborne particles, as well as viable fungal and bacterial microorganisms, were measured in all buildings studied; no associations were found with symptom prevalence.[16] Study 6 reported that increased symptom prevalence was related to factors such as increased temperature and greater amounts of high surface area materials, open shelving, total floor dust, and potentially allergenic floor dust.[26]

Studies 1 through 5 assessed all buildings between November and March; study 6 between February and May.[22]

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*Personal communication, J. Harrison.

**Personal communication, A. Robertson.

***Personal communication, A. Hedge.

Alfred Sommer Named Dean of Hopkins School of Public Health

Alfred Sommer, MD, MHS, a distinguished Hopkins ophthalmologist, epidemiologist and specialist in international health, has been named dean of the Johns Hopkins University School of Hygiene and Public Health, effective September 1, 1990. Sommer succeeds Donald A. Henderson, MD, MPH, who has served as dean for 13 years. The School of Public Health is the largest in the world, with more than 300 faculty members and 1,000 students from 75 countries and projects in nearly 40 nations.

Sommer is professor of ophthalmology at the School of Medicine and holds joint appointments in the departments of epidemiology and international health in the School of Public Health. He is internationally recognized for his pioneering work with vitamin A, in which he found that small, inexpensive doses can save the lives of millions of children around the world. Sommer's discovery came as a result of his work using vitamin A to prevent blindness in malnourished children in Indonesia and other developing nations.

A native of New York City, Sommer, 47, received his medical degree from Harvard in 1967 and his master of health science degree from the Hopkins School of Public Health in 1973.

Sommer is an adviser to numerous national and international groups, including the World Health Organization, the National Eye Institute, the Asian Foundation for the Prevention of Blindness, the International Agency for the Prevention of Blindness, Helen Keller International and the Royal Commonwealth Society for the Blind. He is president of the International Federation of Eye Banks and has published more than 180 papers, reviews or book chapters.

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The Association of Corneal Arcus with Coronary Heart Disease and Cardiovascular Disease Mortality in the Lipid Research Clinics Mortality Follow-up Study

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Abstract: The relationship between corneal arcus (arcus senilis) and mortality from coronary heart disease (CHD) and cardiovascular disease (CVD) is examined in a prospective study of White men (n = 3,930) and women non-hormone users (n = 2,139), ages 30–69, followed for an average of 8.4 years as part of the Lipid Research Clinics Mortality Follow-up Study. After excluding those with clinically manifest CHD at baseline, corneal arcus was strongly associated with CHD and CVD mortality only in hyperlipidemic men ages 30–49 years, for whom the relative risk for CHD and CVD death was 3.7 and 4.0, respectively, after adjusting for age, total cholesterol, HDL cholesterol, and smoking status using a Cox proportional hazards model. Among 30–49 year old males, corneal arcus appears to be a prognostic factor for CHD, independent of its association with hyperlipidemia in this age-group, of about the same magnitude as other common risk factors, underscoring the usefulness of corneal arcus as a prognostic factor to the practicing clinician. (*Am J Public Health* 1990; 80:1200–1204.)

Introduction

Corneal arcus is an extracellular lipid infiltration of the peripheral cornea. It appears as a yellowish-white ring around the cornea, and is separated from the limbus by a 0.3 to 1 mm lucid zone.[1–4] These deposits consist mainly of cholesterol, cholesterol esters, phospholipids, and triglycerides.[1,5] Corneal arcus has been described in children,[3,6] but it is more prevalent among older people and therefore has been often called arcus senilis.[1–6] It occurs more often among Blacks than Whites[4,6,7] and tends to appear earlier in life in Blacks than in Whites.[1–4,6,7]

Rifkind and Dickerson[8] found an association of corneal arcus with coronary heart disease (CHD), and pointed out that its characteristics are similar to those of atherosclerotic lesions: both accumulate in relatively avascular tissues, both increase with age, and are more frequent among males. Data from the Western Collaborative Group Study indicated an association of corneal arcus with the incidence of coronary heart disease in men below age 50.[9] Moreover, it has been found to be related to risk factors of CHD such as hyperlipidemia and to occur more often among patients with familial dyslipoproteinemias.[1–3,6–18] However, data from several studies showed no independent relationship between corneal arcus and CHD and suggested that both were related to elevated serum cholesterol levels.[7,8,12,15,17]

Segal, *et al*,[18] examined the data from the Lipid Research Clinics (LRC) Prevalence Study, which is a major source of information on the occurrence of hyperlipidemia in North America, and found an independent relationship between corneal arcus and the prevalence of CHD. We here report on the relation between corneal arcus diagnosed in White participants of the LRC Prevalence Study based on the mortality from CHD and CVD during a mean follow-up of 8.4 years.

Methods

The methods of the Lipid Research Clinics Prevalence Study and of the Lipid Research Clinics Mortality Follow-up Study have been described in detail elsewhere.[19,20] In summary, the following points are relevant for the present analysis.

Prevalence Study

The Prevalence Study was conducted in the period 1972–76 in 10 Lipid Research Clinics in the United States and Canada. In the first survey (Visit 1), 60,502 individuals (out of 81,926 eligibles) representing a wide ethnic, geographic, socioeconomic, and age variation had their plasma levels of cholesterol and triglycerides determined. A 15 percent random sample of all Visit 1 participants, plus all those with high plasma cholesterol or triglyceride levels or who were taking lipid-lowering medications, plus varying (by clinic) proportions of those with borderline elevation in cholesterol or triglyceride, were invited for a more extensive examination (Visit 2). See Appendix for the definition of "high" and "borderline elevated." Overall, 85 percent of the 12,595 persons eligible for Visit 2 were actually examined. The data used in this analysis, except for a Visit 1 hyperlipidemia variable, were obtained at Visit 2.

Follow-up Mortality Study

All men and women who were at least 30 years old at Visit 2 had their vital status determined annually from 1977 through 1983. Mean follow-up was 8.4 years, with a range of 5.7 to 9.9 years. In case of death, cause was classified as coronary heart disease (CHD), cardiovascular disease (CVD), or due to other causes, using standard criteria.[20] For deaths suspected of being caused by CVD, the cases were reviewed by a panel of cardiologists. They analyzed the death certificate and information obtained from the next-of-kin and from hospitalization records if the person was hospitalized within 30 days prior to death, or from the personal physician if there had been no hospitalization within 30 days prior to

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death. Vital status is known for over 99.6 percent of the participants.

Exclusions

Excluded from all CVD analysis were participants with possible or definite CHD at baseline, according to the presence of one of the following: angina pectoris diagnosed by the Rose Questionnaire[21] or during the treadmill test; use of angina medications, antiarrhythmics, digitalis or propranolol; exclusion from the treadmill test because of congestive heart failure, R-on-T type premature ventricular contraction, ventricular tachycardia, parasystolic focus, atrial flutter or atrial fibrillation; or resting ECG evidence of diagnostic or equivocal myocardial infarction.[22] Female users of estrogens or progestogens were excluded because of the small number who had corneal arcus. Black participants were excluded because of small numbers. Individuals invited to Visit 2 because of borderline hyperlipidemia were also excluded for statistical reasons, as explained below, as were individuals invited solely because of use of lipid-lowering medication. Finally, those with nonfasting (<12 hours) or missing lipid values and pregnant women were excluded from the analysis.

Corneal Arcus Diagnosis

The interviewers were trained to identify corneal arcus in the Visit 2 using a uniform protocol.[23,24] They stood in front of the participants so that their eyes were at the same level during the examination, which was usually done in natural (rather than artificial) light, the source of which was tangential to the eye. The upper and lower poles of the eyes were examined. Interviewers were directed to look for a whitish fatty material at the periphery of the cornea. The corneoscleral junction had to be observable for a diagnosis of corneal arcus to be made. For these analyses only positive answers were regarded as indicative of corneal arcus and an "uncertain" response was considered as negative.

Laboratory Methods

A detailed description of the laboratory processing procedures is provided in the LRC Program Laboratory Methods Manual[25] and reviewed elsewhere.[26]

Statistical Methods

Visit 2 sample data are analyzed to draw inferences about a population like that of Visit 1. In order to account in analysis for the sampling scheme, the data are treated as a stratified random sample, with two strata: hyperlipidemics, all of whom were invited to Visit 2, and normolipidemics (including borderline hyperlipidemics), 15 percent of whom were invited to Visit 2. For simplification, the oversampling of borderline hyperlipidemics and of users of lipid-lowering medication were excluded. It should be emphasized that borderline hyperlipidemics were not in general excluded, but only the oversampling invited to Visit 2. Because of the higher proportion of hyperlipidemics in the sample relative to the population, weighting techniques were used in the estimation of overall population parameters.

CHD and CVD mortality rates (deaths per 1,000 person-years of follow-up) were calculated for corneal arcus cases and non-cases, for each age/sex group, by lipid strata and weighted across lipid strata. Confidence intervals or tests of statistical significance are not given for these descriptive statistics, but rather are reserved for the models' fit. Age groups are 30–49 and 50–69. Similar mortality rates were also calculated with respect to other possible prognostic factors besides corneal arcus. These factors are given below, along with cutpoints which define the categories (greater than or equal to versus less than cutpoint) for which mortality rates were calculated:

- Serum cholesterol level (240 mg/dl).
- Fasting serum triglyceride level (250 mg/dl).
- Low density lipoprotein (LDL) cholesterol level (160 mg/dl).
- High density lipoprotein (HDL) cholesterol level (40 mg/dl).
- Body mass index (BMI) (30 kg/m^2).
- Smoking status (current versus ex- or nonsmoker).
- Family history of coronary heart disease (either at least one parent died of CHD or experienced angina before the age of 60 or at least one sibling died of CHD before the age of 60).
- Graded exercise test (positive ECG showed a significant ST elevation or depression or a significant change in the ST integral value—for details see Gordon, *et al*[27]).
- Ischemia on resting ECG excluding myocardial infarction (either evidence of left ventricular hypertrophy or other significant ischemia; Minnesota codes 3.1-3.3 with 4.1-4.3 or 1-3-1 through 1-3-6, or 2.1, 4.1, 4.2, 5.1, 5.2, 6.1, 8.1, or 8.2).

In considering the effects of possible confounding variables on the relation in males aged 30–49 between corneal arcus and CHD and CVD mortality, survival models were fit by lipid sampling stratum, using Cox proportional hazards models. In addition to arcus status, survival status and baseline age, the following baseline variables were considered: continuous [total cholesterol, LDL cholesterol, HDL cholesterol, alcohol consumption (g/day), body mass index (kg/m^2), systolic blood pressure, triglyceride]; dichotomous [family history of CHD (yes = 1, no = 0), smoking (yes = 1, no = 0)]. These variables were added one at a time to the "basic" model, with survival status the dependent variable and corneal arcus and age independent variables, and discarded if the corneal arcus-survival association was not changed by their inclusion.

Results

For men free of coronary heart disease at baseline, stratified by two age groups and by lipid sampling strata, the prevalence of corneal arcus, the total follow-up time, the mortality rates from CHD and the relative risk are presented in Table 1. In addition, results are given for the two sampling strata combined, with the stratum-specific results weighted to yield estimates of mortality rates for the Visit 1 population. A high relative risk of CHD mortality was associated with the diagnosis of corneal arcus among hyperlipidemic men under 50 years of age but not among older men. Table 2 shows the same trend when mortality from CVD is considered instead of CHD.

In female non-hormone users, the low prevalence of corneal arcus and the small number of CHD and CVD events preclude any kind of analysis in the younger age group; in the older group, where its prevalence and the number of events increase, the same lack of predictive value for CHD and CVD mortality is observed as in the older men (data available on request to authors).

The proportional hazards models of time to CHD or CVD death (Table 3) show that corneal arcus is an independent prognostic factor for mortality from CHD or CVD in men ages 30–49 years in the hyperlipidemic sampling stratum; for normolipidemic younger men its presence does not appear

TABLE 1—Estimated CHD Mortality Rates (deaths per 1000 person-years of follow-up) by Age Group and Corneal Arcus Status, Excluding Those with Prior Manifestations of CHD: Males

Age (years)	Sampling Stratum	Corneal Arcus Status	N	Number CHD Deaths	Total Follow-up Time (person-years)	Estimated CHD Mortality Rate	Estimated Relative Risk
30–49	Hyperlipidemic	No	1315	10	11237.6	0.89	6.7
		Yes	85	4	675.1	5.93	
	Normolipidemic	No	1202	8	10339.5	0.77	3.4
		Yes	46	1	377	2.65	
	Total*	No	2517	18	21577.1	0.79	4.7
		Yes	131	5	1052.6	3.74	
50–69	Hyperlipidemic	No	311	13	2504.2	5.19	0.0
		Yes	68	0	583.1	0.00	
	Normolipidemic	No	597	18	5031.9	3.58	0.9
		Yes	115	3	947.5	3.17	
	Total*	No	908	31	7536.16	3.64	0.8
		Yes	183	3	1530.6	2.99	

*Mortality rates weighted across sampling strata.

TABLE 2—Estimated CVD Mortality Rates (deaths per 1000 person-years of follow-up) by Age Group and Corneal Arcus Status, Excluding Those with Prior Manifestations of CHD: Males

Age (years)	Sampling Stratum	Corneal Arcus Status	N	Number CHD Deaths	Total Follow-up Time (person-years)	Estimated CHD Mortality Rate	Estimated Relative Risk
30–49	Hyperlipidemic	No	1315	13	11237.6	1.16	6.4
		Yes	85	5	675.1	7.41	
	Normolipidemic	No	1202	14	10339.5	1.35	2.0
		Yes	46	1	377	2.65	
	Total*	No	2517	27	21577.1	1.32	3.2
		Yes	131	6	1052.1	4.23	
50–69	Hyperlipidemic	No	311	22	2504.2	8.79	0.0
		Yes	68	0	583.1	0.00	
	Normolipidemic	No	597	26	5031.9	5.17	1.0
		Yes	115	5	947.5	5.28	
	Total*	No	908	48	7536.2	5.31	0.9
		Yes	183	5	1530.6	4.98	

*Mortality rates weighted across sampling strata.

TABLE 3—Estimated CHD and CVD Hazard Ratio, Comparing Subjects with Corneal Arcus to Those Without; Adjusted for Age, Total Cholesterol, HDL-C, and Smoking*, Men Aged 30–49 Years

Lipid Stratum	CHD Hazard Ratio	(95 Percent Confidence Interval)	CVD Hazard Ratio	(95 Percent Confidence Interval)
Hyperlipidemic	3.7	(0.9,14.7)	4.0	(1.2,12.9)
Normolipidemic	2.2	(0.3,20.1)	1.3	(0.2,10.4)

*LDL-cholesterol, alcohol consumption, BMI, systolic blood pressure, and triglyceride were also considered, but had no effect on the C.A./survival association, so were discarded.

to be of the same importance. The covariates included are age and those whose inclusion in the model substantially modified the estimates of relative hazard of CHD or CVD mortality as related to corneal arcus. These covariates are total cholesterol, HDL-cholesterol, and smoking. With or without these additional covariates the relative hazards are similar for normolipidemics, but for hyperlipidemics the relative hazards adjusted for age alone are about 1.6 times those for models presented in Table 3.

The relative risk of the diagnosis of corneal arcus in the 30–49 year old male group is compared in Table 4 to that of other possible risk factors. As can be seen there, corneal arcus appears to be at least as statistically strong a prognostic factor for CHD as obesity, hypo-HDL, ischemia on resting ECG, hypertriglyceridemia and family history of CHD, and not very different in magnitude from the relative risk from smoking habit, hypertension, hyper-LDL, and hypercholesterolemia. Details concerning this relation are given in Segal, *et al.*[18]

Discussion

In men under 50 years of age, corneal arcus has been shown in a prospective study to be a predictor of CHD

TABLE 4—Estimated Mortality Rates (per 1000 person-years) and Relative Risks of Death from CHD in Asymptomatic Men Aged 30–49 Years, by CHD Risk Factor Status

		Hyperlipidemic Stratum		Normolipidemic Stratum		Population Estimates*	
Risk Factor	Status	Death Rate	Relative Risk	Death Rate	Relative Risk	Death Rate	Relative Risk
Corneal Arcus	Yes	5.93	6.66†	2.65	3.44	3.74	4.73
	No	0.89		0.77		0.79	
Current Smoker	Yes	2.00	4.26††	1.72	5.73††	1.78	5.56††
	No	0.47		0.30		0.32	
Quetelet Index	≥30	1.27	1.55	0.96	—	1.00	3.57
	<30	0.82		—		0.28	
Hypertensive	Yes	1.96	2.33	2.68	7.66††	2.48	5.90††
	No	0.84		0.35		0.42	
LDL-C Level	≥160	1.84	3.61††	3.33	9.79††	2.39	6.83††
	<160	0.51		0.34		0.35	
HDL-C Level	<40	1.76	2.71†	1.66	3.95†	1.68	3.73††
	≥40	0.65		0.42		0.45	
Ischemia on Exercise ECG	Present	9.79	9.79	10.00	14.29	9.94	13.25
	Absent	1.00		0.70		0.75	
Ischemia on Resting ECG	Present	7.64	7.64	2.15	2.56	2.70	3.14
	Absent	1.00		0.84		0.86	
Cholesterol Level	≥240	2.19	—	5.21	12.71††	2.59	6.64
	<240	—		0.41		0.39	
Triglyceride Level	≥250	1.73	1.94	2.37	3.04	1.78	2.25
	<250	0.89		0.78		0.79	
Family History of CHD	Present	2.17	2.44	0.96	1.17	1.21	1.46
	Absent	0.89		0.82		0.83	

*Weighted across sampling strata.
†0.05 < p < 0.10, two-sided test.
††0.01 < p < 0.05, two-sided test.

mortality, independent of presence of hyperlipidemia, and a stronger predictor for hyperlipidemics. Above the age of 50 its diagnosis does not appear to be positively related to the subsequent manifestation of a fatal CHD event. These findings help to clarify previous discussion about this relation,[7,28] confirming the observations made in retrospective,[8,29] cross-sectional,[18,30] and prospective studies.[9] They are in agreement with the interpretation that corneal arcus and coronary atherosclerosis share common determinants in young men, while local factors are more important for its occurrence in older persons.[8,12]

The findings in women confirm the low prevalence of corneal arcus in the young age group,[30,31] which with the low mortality rates rules out the possibility of drawing conclusions about its relation to CHD and CVD mortality. In the older group, where the prevalence of corneal arcus and the mortality rate increase, there is the same lack of relation observed in older men.

The ability to detect patients at high risk of CHD has been of continuous concern, considering the frequent presentation of the disease as sudden death[32] and its devastating consequences, especially in the families of young men. The magnitude of the corneal arcus risk in this age group compared to other usual screening tests (Table 4) highlights the utility of this simple and inexpensive tool as a prognostic factor and reinforces the importance of its diagnosis during the physical examination. This is noteworthy, considering that it had lower prevalence in the baseline of this population-based cohort than in some studies which used hospitalized or referred patients. The fact that, in this study, corneal arcus was detected only by a single examination, without the use of slit lamp, could have resulted in some misclassification.[17] However, such misclassification would be independent of either lipid status or later CHD mortality, so would only bias our results toward the null, that is, toward finding no association between it and CHD mortality. The association between corneal arcus and hyperlipidemia *alone* would suggest evaluation of the lipid profile of young men with corneal arcus. The findings in this paper indicate that it also may be prudent to suggest that all young patients with corneal arcus should undergo a detailed evaluation of their other CVD risk factors.

APPENDIX

Age-Specific Cutpoints Used for Selecting Participants for Visit 2

	Cholesterol (mg/dl)*		Triglyceride (mg/dl)**	
Age Group	Borderline Cutpoint	Elevated Cutpoint	Borderline Cutpoint	Elevated Cutpoint
30–39	220	240	150	250
40–49	225	260	150	300
50–59	245	280	150	300
60+	245	280	150	300

*Conversion factor to SI Units (mmol/L): 0.02586
**Conversion factor to SI Units (mmol/L): 0.1129

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Environmental Tobacco Smoke Exposure during Infancy

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Abstract: We collected information about household smoking habits from 518 mothers when they made their first well child visit with a 6 to 8-week old infant. A urine sample was also collected from the infant, the cotinine concentration measured, and the measurement correlated with data provided by the mother. Eight percent of the infant urine cotinine values fell at or above 10 μg/L in the 305 households where no smoking was reported. Corresponding rates were 44 percent in the 96 households where a member other than the mother smoked, 91 percent in the 43 households where only the mother smoked, and 96 percent in the 74 households where both the mother and another household member smoked. In households where the mother smoked, infant urine cotinine levels were lower in the summer, and higher when the infant was breast-fed. A screening question about family smoking habits in conjunction with well child care could effectively define a group of infants exposed to environmental tobacco smoke and thus be at greater risk for respiratory diseases. (*Am J Public Health* 1990; 80:1205–1208.)

Introduction

Infants and young children chronically exposed to environmental tobacco smoke (ETS) have a higher risk of developing acute respiratory illnesses than their unexposed counterparts, and hospitalization is more often necessary to manage these conditions.[1–4] The studies defining this risk relied upon family reporting (usually by the mother) of numbers of cigarettes smoked in the household and other locations where the infant or child might be exposed. The availability of biochemical markers capable of measuring tobacco smoke products quantitatively in blood, saliva, and urine now offers the opportunity to obtain a more accurate estimate of actual tobacco smoke absorption by infants and children, irrespective of location. Cotinine, a metabolic derivative of nicotine, has proven particularly useful, because it is chemically stable, is not found in nature (thereby avoiding false-positive test results), can be measured reliably in non-smokers exposed to ETS, and has a circulating half-life of about one day.[5,6] Greenberg, *et al*,[7,8] have recently reported their observations on urine cotinine levels in infants exposed to ETS, documenting the relation between self-reported exposure and urine cotinine levels. The present report provides further data on this relation, based on analyses from a large, population-based study focused on 6 to 8-week-old infants receiving routine well child care in private physician offices and clinics in a mid-sized city in the United States.

Methods

Patient Population

Thirty-seven physicians in the greater Portland, Maine area were asked to participate in the study, and 30 (81 percent) agreed to take part; both of the well child clinics also participated. Following informed consent 518 infant/mother pairs were enrolled at their first well child visit between January and October 1988. Each participating mother answered questions about her age, years of completed education, occupation for both herself and the father, ages of other children, breast-feeding, smoking, number of cigarettes smoked, and smoking habits of others in the household. The age of infants at enrollment was between 6 and 8 weeks. The mean age of mothers in the study was 27.4 years, and they had completed, on average, 13 years of school. For 50 percent of the mothers, this was their first child. To examine the extent to which the study sample represented the childbearing population of Greater Portland, Cumberland County data were analyzed in a 70 percent subset of the county's pregnancies in 1987, all of whom had maternal serum alpha-fetoprotein screening. For both groups, 99 percent were White and average age was 27 years; 9 percent of the study population were not high school graduates compared to 11 percent of the county population.

Urine Collection and Cotinine Assay

It was explained that the urine sample was to be analyzed to learn more about environmental exposures, but cigarette smoke exposure was not specifically mentioned. Two cotton rolls were placed in the diaper at the beginning of the office visit. They were either removed and placed in the glass screw-top specimen vial (if wet) at the end of the office visit or mailed back by the mother if urination had not occurred. This method of urine collection in no way alters the concentration of urine constituents, such as creatinine, and the rate of evaporation of liquid is negligible.[9] Approximately half of the samples were obtained during the office visit. Nine percent of the samples were unsatisfactory for analysis, either because of stool contamination or inadequate volume, and in 81 percent of those cases a repeat urine sample was successfully obtained. Before assaying, the urine was transferred to a test tube by compressing the cotton rolls inside a disposable syringe.

The urine was assayed for cotinine by a competitive radioimmunoassay, using cotinine antiserum raised in rabbits and an iodine ^{125}-label described previously.[10,11] The standard curve of the procedure ranged from 0.25 to 12.0 μg/L, with an estimated lower limit of sensitivity of 0.2 μg/L. A dose-response relationship down to 0.3 μg/L has previously been demonstrated between serum cotinine and ETS exposure with this assay.[10] The lower limit of 1.0 μg/L was selected for detecting urine cotinine, however, to allow for possible assay variability within the 0.25 to 1.0 μg/L range that might result from differences in urine composition and

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pH. Consequently, all values below 1.0 µg/L in the present study are assigned a value of <1.0 µg/L.

Results

Figure 1 contains a scatterplot distribution of urine cotinine levels. Among 305 infants who were not exposed to household tobacco smoke, cotinine levels from 97 (32 percent) fell below 1.0 µg/L, and another 185 (60 percent) fell between 1.0 and 9.9 µg/L. Urine cotinine values of 10 µg/L and above were found in only 23 of the infants (8 percent). Overall, the median urine cotinine level in this group was 1.6 µg/L.

Among 96 infants with ETS exposure from other household members only, the median level was 8.9 µg/L; among 43 infants with ETS exposure from the mother only, the median level was 28 µg/L; among 74 infants with ETS exposure from both the mother and other household members, the median level was 43 µg/L. Cotinine values falling at or above 10 µg/L in those categories were: 44, 91, and 96 percent, respectively. The horizontal line drawn at 10 µg/L in Figure 1 represents a reasonable estimate of significant ETS absorption; 94 percent of the infants whose mother smoked had values above this level, as opposed to only 8 percent of the infants in the unexposed category.

Breast Feeding in Relation to Infant Cotinine Levels

Figure 1 also identifies infants who were breast fed (open circles) and those who were bottle fed (closed circles). Among the 401 mothers in the study who did not smoke, 207 (52 percent) breast fed, as opposed to 16 (14 percent) of the 117 mothers who smoked. In households where the mother smoked, breast feeding was associated with significantly higher infant urine cotinine levels, both in the presence of other smokers in the household (urine cotinine medians = 213 µg/L with breast feeding and 39 µg/L without breast feeding, 2-sided t-test on $\log_{10}$ transformed cotinine level, $p = 0.003$), and in the absence of other smokers in the household (urine cotinine medians = 87 µg/L and 25 µg/L, $p < 0.001$).

After excluding breast feeding, regression analyses were performed to examine the relation between number of cigarettes smoked by the mother (exposure) and $\log_{10}$ of the infant urine cotinine level (absorption) both in households where only the mother smoked and in households where others smoked as well. Absorption was related to exposure in both groups (regression coefficient = 0.0155, SE = 0.0068, in the 35 households where only the mother smoked) (regression coefficient = 0.0185, SE = 0.0046, in the 66 households where both the mother and other household members smoked). In both groups, the infant urine cotinine levels differed by a factor of approximately two over the range of exposure.

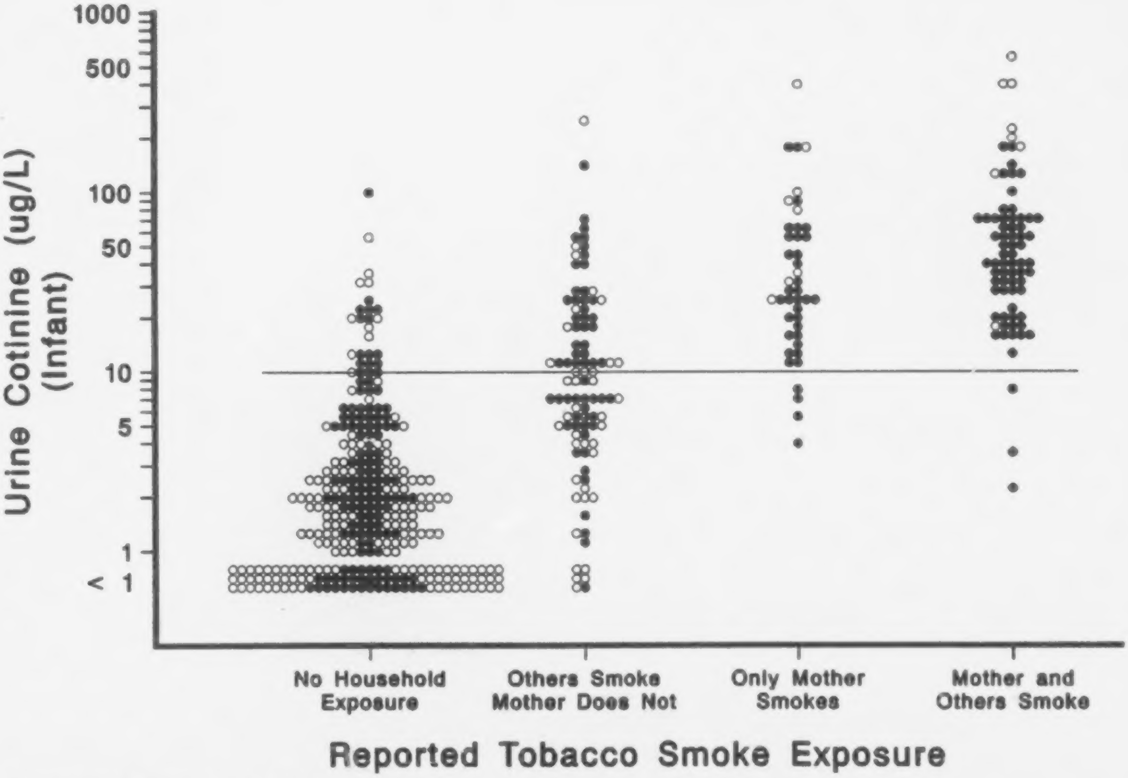

FIGURE 1—Urine Cotinine Levels in Infants, According to Environmental Tobacco Smoke Exposure in the Home.
Cotinine measurements are in spot urine samples. Closed circles indicate that the infant is not breast fed; open circles indicate breast feeding. Cotinine measurements < 1.0 µg/L are considered undetectable, and the horizontal line drawn at 10 µg/L is the cutoff defined from data in the study to indicate significant ETS absorption. Median urine levels in the four groups are as follows: no household exposure—1.6 µg/L; others smoke, mother does not—8.9 µg/L; only mother smokes—28 µg/L; mother and others smoke—43 µg/L.

Influence of Season of the Year on Urine Cotinine Levels in Smoking Households

Table 1 shows, in households where the mother smoked, that the median, 25th, and 75th centiles for infants' urine cotinine levels were significantly lower in the summer (2 sided t-test on $\log_{10}$ transformed cotinine levels, $p = 0.03$); this could not be explained either by the presence of other smokers in the household or by the number of cigarettes smoked by the mother. Preliminary analysis demonstrated no differences between winter, spring, and fall, and so these were combined in the table.

Discussion

Table 2 compares selected characteristics of the present population with those of the population studied by Greenberg, *et al.*[8] The infants in the present study were, on average, 31 days older at enrollment and were primarily Caucasian. The ages, numbers of cigarettes smoked by the mothers, and rate of breast-feeding in mothers who smoked were similar in the two studies. A greater proportion of women in the present study group had finished high school. Greenberg, *et al*, found that infant urine cotinine concentrations were at or above 2 μg/L in 60 percent of their subjects, as compared with 64 percent in the present study, and median cotinine values were also similar (9 and 11 μg/L, respectively) in infants who were not breast fed.

Breast feeding has already been reported to influence infant urine cotinine levels among mothers who smoke,[12,13] and the present study provides further documentation of that effect. Breast milk from mothers who smoke contains high levels of cotinine, and it is likely that ingestion and absorption of cotinine (and also nicotine) explains why breast fed infants of smoking mothers have higher urine cotinine levels than when the mother does not breast feed. Cotinine from this source carries different implications from cotinine produced from inhaled tobacco smoke and needs to be taken into account when using cotinine results to estimate ETS absorption. In the present study household ETS was not reflected in raised infant urine cotinine levels via ingestion in breast fed infants, when the mother did not smoke.

Data from the present study provide evidence, for the first time, of a seasonal influence on infant urine cotinine levels. The lower median cotinine level in infant urine samples during the summer from households where the mother smoked suggests that increased outdoor activity, better ventilation, or a combination, might play a role. When interpreting urine cotinine values, this phenomenon needs to be taken into account, since the average yearly exposure to ETS may be underestimated during the summer months. This variable may behave differently in different climates.

Studies in adults indicate that urine cotinine levels are approximately 10 times higher than those in serum, both in smokers and non-smokers.[10] Since the urine cotinine value reflects exposure over several days, urine cotinine measurements appear suitable both for assessing degree of ETS-related risk and for measuring success following intervention to reduce ETS exposure. The cotton-roll method of urine collection employed in this study is particularly suited for use in the practitioner's office as part of either clinical investigation or ongoing health care counseling.

TABLE 2—A Comparison of Household Smoking Habits and Infant Urine Cotinine Levels in the Present Study and a Recently Published Study

	Greenberg et al[8]	Present Study
Number of Infants	433	518
Average Infant Age at Enrollment (days)	18	49
White (%)	65	99
Mother not High School Graduate (%)	26	9
Mother Smokes (%)	27	23
Average Age of Mother (years)	25	27
Average Cigarettes Smoked/Day By Mother	14	17
Mother Smokes and Breastfeeds (%)	18	14
Household Member Smokes (%) (includes mother)	55	41
Infant Cotinine Value ≥2 μg/L (%)	60	64
Median Cotinine Level for Values ≥2 μg/L (Range)	9 (2–138)	11 (2–261)
Correlation of Mother's Number of Cigarettes versus Infant's Urine Cotinine (r_s value)	0.54	0.39

Our results suggest that a screening question about household smoking habits effectively defines a group of infants with urine cotinine levels of 10 μg/L or above. In our study, 86 percent of all infants with urine cotinine levels at or above 10 μg/L were found in the 41 percent of households where the mother indicated that either she or other household members smoked. Families in which any household member smokes might be considered suitable candidates for further documentation of the extent of infant absorption of ETS. Before implementing this type of approach, however, techniques for teaching families how to avoid infant ETS exposure need to be developed and evaluated.

ACKNOWLEDGMENTS

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TABLE 1—Urine Cotinine Levels in Infants Whose Mothers Smoke, According to Season of the Year*

Season	Number of Infants	Number of Cigarettes Mother Smoked (Mean)	Other Smokers in the Household (%)	Urine Cotinine (μg/L) Centile		
				25th	50th	75th
Winter/Spring/Fall	74	18	68	22	39	64
Summer	27	17	59	15	24	55

*Excludes 16 breast feeding infants

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Drinking Water Contamination and the Incidence of Leukemia: An Ecologic Study

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Abstract: An ecologic study was performed to examine the relation between the incidence of leukemias and the occurrence of volatile organic chemical (VOC) contamination of drinking water supplies within a study area comprised of subpopulations differentially exposed to drinking water VOCs (trichloroethylene and related solvents). Populations served by community water supplies were classified into exposure categories according to VOC contamination status based on 1984–85 sampling data. Leukemia incidence data (1979–84) were collected from a population-based cancer registry. For females, the standardized incidence ratio was elevated only in towns in the highest of three exposure categories. No association was observed in males in any of the exposure categories. A Poisson regression analysis of the data, using finer exposure strata, indicated an increase in risk among females with increasing level of contamination which appeared to be distributed evenly across all age strata. The rate ratio for females at the highest exposure stratum for total non-THM VOCs compared to the least exposed stratum was 1.68. The observed association appears to suggest that drinking water contaminated with VOCs may increase the incidence of leukemia among exposed females, but caution is advised in the interpretation of these results because of the uncertainties inherent in ecologic studies. (*Am J Public Health* 1990; 80:1209–1212.)

Introduction

Since the middle 1970s, there has been considerable epidemiologic interest in the relation between organic contaminants in drinking water and increased cancer incidence in exposed populations. The focus of several studies has been on chlorinated compounds that can form in relatively high concentrations following chlorination of surface water for disinfection. These compounds, some carcinogenic or mutagenic, include the volatile trihalomethanes (THMs) and many nonvolatile substances. There is some evidence that consumption of chlorinated surface water is related to an increased risk of bladder and possibly colorectal cancers.[1–4]

Groundwater was long thought to be relatively protected from such contamination. However, national and state surveys have demonstrated that numerous groundwater supplies throughout the nation have contained volatile organic compounds (VOCs) other than THMs,[5,6] in particular the halogenated solvents trichloroethylene (TCE), tetrachloroethylene (perchloroethylene or PCE), and 1,1,1-trichloroethane (TCA).

In Woburn, Massachusetts, an association was reported between the pattern of VOC water contamination (TCE and others) and the incidence of childhood leukemia.[7] Further epidemiologic analysis of the pattern of non-THM VOC water contamination and the incidence of leukemias is warranted in other geographic areas.

In New Jersey, routine semi-annual testing for 14 VOCs including halogenated solvents has been required of public community water systems since late 1984.[8] Results from 1984 and 1985 showed that about 18 percent of the state's 620 water systems, estimated to serve approximately 20 percent of the state's population, contained detectable levels of non-THM VOCs.[9,10] Data on THM concentrations are also available.

We performed a study of the possible relation between the incidence of leukemia and VOC contamination of drinking water in the state of New Jersey.

Methods

Study Population

In an ecologic study, an ideal geographic area would be completely served by community water systems for which monitoring data are available and would contain subunits that experience a range of contaminant concentrations to ensure exposure differences. The study area that best met these criteria consisted of towns completely within an area bounded by the Lower Passaic River and Saddle River drainage basins. The area is almost completely served by public water supplies, many of which have tapped VOC contaminated groundwater, while others utilize groundwater or surface water free of detectable levels of non-THM VOCs. This portion of the state is primarily urban and residential so that town coding in the Cancer Registry is likely to be accurate, i.e., mailing address and actual residence are likely to be the same.

Towns within the study area were excluded if less than 90 percent of the population was served by public water systems. The age- and sex-specific populations of each municipality were obtained from 1980 US Census summaries.

Exposure Measurement

The New Jersey Department of Environmental Protection compiled all sampling results for each water system serving populations in the study area. The drinking water quality data included the 14 VOCs under the state's monitoring requirements from 1984 and 1985, and THM analyses from 1984 and 1985.

The Department also provided other available sampling data, information on extent of distribution systems, well or reservoir use, and patterns of water purchases among systems so that the water supply of each town could be characterized. Any significant changes in water supply and use patterns in the past decade were noted.

For each water system, we calculated the mean chemical-specific concentrations of VOCs and THMs in distribution system samples for the period 1984–85. Although data were available for later years, the first rounds of monitoring were thought to be more representative of past exposure since corrective actions were taken by many water systems

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TABLE 1—Exposure Classification, Number of Reported Leukemia Cases 1979–84, and Population by Gender

Non-THM VOC rating for SIR	Exposure Stratum for regression (μg/l)*	Leukemia Cases (population)		Number of Towns
		Males	Females	
++	72	1 (5,125)	4 (5,616)	1
	67	5 (11,346)	8 (12,610)	1
	47	0 (1,973)	0 (2,156)	1
	40	8 (12,699)	9 (14,104)	1
	37	11 (8,539)	7 (9,661)	1
		25 (39,682)	28 (44,147)	5
+	12	13 (15,546)	7 (16,683)	1
	9	7 (17,583)	14 (20,738)	1
	7	5 (5,314)	5 (5,488)	1
	5	13 (28,508)	10 (31,078)	4
		38 (66,951)	36 (73,987)	7
–	3	6 (8,358)	3 (8,836)	2
	2	7 (9,385)	4 (10,302)	2
	1	103 (161,195)	74 (182,053)	9
	0	29 (38,478)	19 (44,681)	2
		145 (217,416)	100 (245,872)	15

*Sum of average non-THM VOC concentrations in 1984–85 samples.

following the initial results. The number of distribution system samples for each supply varied from two to 50 in the period. Values for each non-THM VOC, total non-THM VOCs, and total THMs were then assigned to each town based on the water supplies that serve that town.

Disease Measurement

Incident cases of leukemias for the towns within the study area were collected from the New Jersey Cancer Registry for the six-year period 1979–84. Information on each case included date of diagnosis, age at diagnosis, town of residence at time of diagnosis, race and sex, and histologic type according to the International Classification of Diseases for Oncology.[11]

Data Analysis

Based on the 1984–85 contaminant values, towns were categorized as to contaminant status for total non-THM VOCs and for THMs. Categorical exposure levels were defined for each variable, empirically derived from inspection of the distribution of values. For each categorical exposure variable, incidence data for the towns within an exposure category were pooled, and standardized incidence ratios for the combined town groups were calculated. Expected incidence for the grouped areas were derived by applying New Jersey statewide 1982 age-sex-specific rates of total leukemias to the pooled 1980 age-sex-specific populations.[12] (Age-sex-specific rates for specific histologic types are not available.) Standardized incidence ratios (SIRs) were calculated by dividing the observed number of cases by the expected number for each town grouping. The 95% confidence intervals of the SIRs were estimated.[13]

Towns sharing the same values for non-THM VOCs were pooled into exposure strata. For each gender, the number of leukemia cases (total and type-specific) in each exposure stratum and age-group specific population was fitted to a log-linear regression model assuming a Poisson distribution of the counts. Separate regression models were developed for total non-THM VOC and for TCE and PCE, two subsets of that variable.[14,15] Predictor variables included in the models were age group (0–19, 20–49, and 50+) and exposure stratum; interactions were also included. Rate ratios were calculated from the parameters generated by the models. Analysis was performed using the GLIM software package.[16] A hierarchical backward elimination method[17] was used to determine final models.

Results

Three of the 30 towns originally contained in the study area were excluded since approximately 50 percent, 4 percent, and 1 percent of their population, respectively, was served by public community water supplies. Approximately 95 percent to 100 percent of the populations in each of the remaining 27 towns in the study area are served by public community water supplies. These 27 towns contained 688,055 persons (324,049 males and 364,006 females), or 9.3 percent of the population of New Jersey in 1980.

Table 1 includes mean total non-THM VOC values assigned to each town or group of towns for the SIR analysis. TCE, PCE, TCA, and dichloroethylenes (DCE) comprised nearly all of the non-THM VOC. Based on inspection of the average values for each town, three categories of total non-THM VOC status were formed: ++ (72–37 ppb), + (12–5 ppb), or – (3 to less than 1 ppb). Two categories of THM status were also formed: + (76–25 ppb) or – (4–1 ppb).

Figure 1 displays the geographic pattern of this categorization. For THMs, 19 towns were rated plus (+) and eight were rated minus (–).

Over the six-year period 1979–84, 208 leukemia cases occurred among males and 164 among females in the entire study area (Table 1). The most frequently reported histologic type among younger age groups of both sexes was acute lymphocytic leukemia (ALL). Among older age groups, chronic lymphocytic leukemia (CLL), acute granulocytic leukemia (AGL), and chronic granulocytic leukemia (CGL)

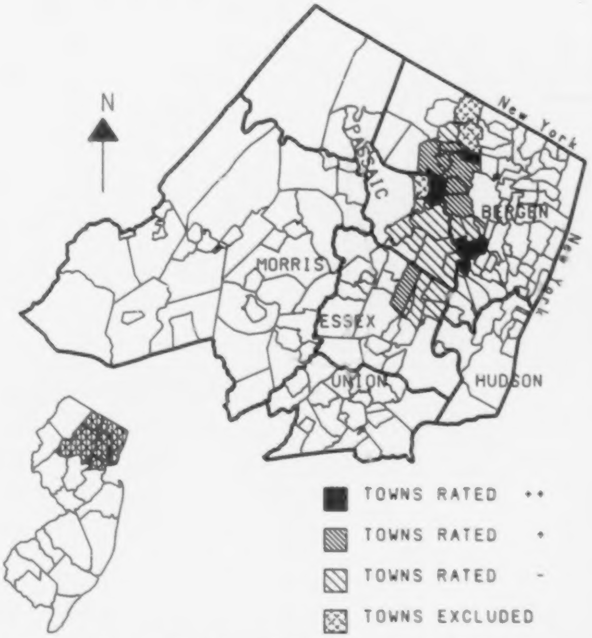

FIGURE 1—Pattern of Total Non-THM VOC Contamination in the Study Area as Categorized for the SIR Analysis

were most frequently reported. Few cases of acute monocytic leukemia were reported, and all were among older males. Twenty-eight percent of the reported cases were coded without specifying histology.

For the entire study area, the observed number of leukemia cases from 1979–84 did not differ from the expected number for either males or females. Among towns classified as ++ for total non-THM VOCs, however, the incidence of leukemia was elevated among females but not in males (Table 2).

No elevation of leukemia incidence was observed for groups of towns classified as either (+) or (−) for THM status among males or females (Table 2).

Regressions were performed for both sexes including categorical age and water quality variables. Results are reported in detail here for females only. The final models of the regression analysis for total leukemias in females (Table 3) do not contain interaction terms between age groups and contaminant status as no p values less than 0.05 were obtained.

The sum concentration of all non-THM VOCs was a statistically significant predictor of total leukemia incidence, adjusted for age. The coefficient for total VOCs was 0.0072 (S.E. = .0039), and is interpreted as the natural logarithm of the increase in the rate ratio per unit increase in exposure. Thus, for the maximum town average total non-THM VOC concentration observed in the study, 72 $\mu g/l$, the rate ratio would be $\exp[(72\ \mu g/l)(.0072)] = 1.68$.

Modeled separately, the age-adjusted coefficients for TCE and PCE concentration were 0.012 (S.E. = .0067) and 0.035 (S.E. = .021), respectively. At the maximum town average TCE and PCE concentrations observed in the study, the rate ratios would be $\exp[(46\ \mu g/l)(.012)] = 1.74$ and $\exp[(16\ \mu g/l)(.035)] = 1.75$, respectively.

When the more common histologic types of leukemia (ALL, CLL, AGL, and CGL) were examined separately, the coefficients for total non-THM VOCs were all of similar direction and magnitude (ALL: 0.016; CLL: 0.0095; AGL: 0.010; CGL: 0.012). There were few cases of each histologic type, hence little power to detect meaningful associations.

TABLE 2—Standardized Incidence Ratios (SIRs) among Males and Females for Groups of Towns Classified According to Various Exposure Categories (Number of cases, 1979–84)

Exposure Category	Number of Cases: Observed	Number of Cases: Expected	SIR	(95% Confidence Interval)
Males				
All towns	208	195.7	1.06	(0.92–1.21)
Total non-THM VOCs—1984–85				
++	25	25.0	1.00	(0.65–1.47)
+	38	40.7	0.93	(0.66–1.28)
−	145	130.0	1.12	(0.94–1.31)
Trihalomethanes—1984–85				
+	177	168.5	1.05	(0.90–1.22)
−	31	27.3	1.14	(0.77–1.61)
Females				
All Towns	164	146.8	1.12	(0.95–1.30)
Total non-THM VOCs—1984–85				
++	28	18.3	1.53*	(1.02–2.21)
+	36	30.3	1.19	(0.83–1.65)
−	100	98.2	1.02	(0.83–1.24)
Trihalomethanes—1984–85				
+	140	126.8	1.10	(0.93–1.30)
−	24	20.1	1.20	(0.77–1.78)

*Statistically elevated SIR ($p < 0.05$)

TABLE 3—Poisson Regression Analysis: Final Models for Total Leukemia Cases among Females

Model	Coefficient	Standard Error
	Exposure: Total non-THM VOCS	
Intercept	−1.85	(0.25)
AGE(20–49)	−0.022	(0.32)
AGE(50+)	1.78	(0.27)
TOTAL VOCS	0.0072	(0.0039)
	Exposure: TCE Concentration	
Intercept	−1.83	(0.25)
AGE(20–49)	−0.021	(0.32)
AGE(50+)	1.78	(0.27)
TCE	0.012	(0.0067)
	Exposure: PCE Concentration	
Intercept	−1.85	(0.25)
AGE(20–49)	−0.019	(0.32)
AGE(50+)	1.78	(0.27)
PCE	0.035	(0.021)

Discussion

Results suggest an association between the contamination of drinking water supplies with non-trihalomethane volatile organic chemicals and an increased incidence of leukemias among females. Because of limitations inherent in the study design, a statement of causal inference cannot be made with confidence at this time.

Ecologic studies are practical because they are quick and inexpensive, but because data reflect the group rather than the individual, the results are best used to develop rather than test etiologic hypotheses. Ecologic studies are susceptible to bias in the estimation of effect if there are factors operating at the individual level that are not accounted for in an aggregate exposure assessment. Additionally, at the group level, the degree of correlation among various predictor variables (multicollinearity) is likely to increase, so that the independent effects of predictors may be difficult to isolate. Potential biases and multicollinearity in ecologic studies can be minimized by using narrow exposure strata and regression to estimate effect.[18]

Misclassification of exposure may exist at both the population and at the individual level. In this study, exposure information (1984–85) was collected at the end of the case collection period (1979–84). Although sampling data prior to 1984 are limited, it was our judgment that these data are reasonable proxies for actual levels years earlier. Since the latency period of chemically-induced leukemias can be relatively short—as little as five years or less for benzene[19]—the problems associated with using exposure information gathered after the development of disease may be lessened.

Within a given population classified according to exposure, there may be significant variability of actual exposure to water-borne contaminants experienced by individuals. Individual-level data on personal tap-water use, residential history and migration patterns, and location of workplace or schools compared to residence were not available for this study.

Additionally, confounding variables such as occupational exposures or local toxic air emissions that may be causally related to the development of leukemias, may be correlated with the pattern of water contamination in the study area. However, each town grouping contained towns with both low and high air emission estimates from the recently available USEPA Toxics Release Inventory database.[20]

At least two of the common contaminants, TCE and PCE, have been shown to be carcinogenic in experimental animal studies, indicating the potential to be carcinogenic in humans.[21–25]

Observations in humans exposed to TCE and PCE or related solvents have not demonstrated a consistent association with leukemias. Studies of the mortality experience of dry cleaning workers have variously reported statistically elevated deaths from a variety of cancer sites. Mortality from leukemia was elevated (but not statistically significant) in one of the studies.[26] In a case-referent study of childhood leukemia, fathers' exposure to chlorinated solvents was associated with excess leukemia in the children.[27]

For TCE and PCE, it has been estimated that daily exposures from these chemicals in the ambient air of New Jersey amount to an average of 90 micrograms per day.[28] Using standard assumptions of drinking water consumption,[29] and assuming an equivalent dose from inhaling volatilized contaminants, drinking water concentrations greater than about 20–25 μg/l would add 80–100 μg of exposure, a doubling of the average daily exposure. This estimate illustrates that drinking water can be an important relative source of exposure at levels encountered in some water supplies.

Although we have analyzed total leukemias in this study, we recognize their clinical and etiologic diversity. Known or suspected risk factors include certain genetic traits (particularly for CGL and CLL), ionizing radiation (apparently most types but CLL), infectious agents, and chemicals such as benzene (primarily AML).[30,31] Combining histologic types together in this ecologic analysis may have obscured an effect if the hypothesized etiologic agent, VOC-contaminated drinking water, is specific to a particular histologic type. A detailed analysis of type-specific incidence in this study was precluded by the small number of cases.

The inconsistency of association with respect to gender in this study cannot be explained given the data and level of analysis used in this study.

Our results suggest that a relation may exist between leukemia incidence and VOC contamination of drinking water, at least among females, although this ecologic study cannot lead to a causal inference. Since the observed association may reflect an underlying causal relation, the potential public health importance warrants further study. In particular, a case-referent epidemiologic study would allow an analysis of several potential risk factors and several histologic types that could not be assessed in this ecologic study.

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Health Status of Migrant Farmworkers: A Literature Review and Commentary

George S. Rust, MD, MPH

Abstract: I made a computerized search of MEDLINE files from 1966 through October 1989 followed by a review of this literature. Four hundred eighty-five articles were scanned; 152 were found specifically related to migrant families, while another 51 articles addressed the health of agricultural workers or farmers in general. Solid data exist on dental health, nutrition and, to a lesser extent, childhood health. Data also were prominent in several disease categories including certain infectious diseases, pesticide exposures, occupational dermatoses, and lead levels in children.

Estimates of the size of the migrant and seasonal farmworker population vary widely. Basic health status indicators such as age-related death rates are unknown. Prevalence rates of the most common cause of death in the United States have yet to be studied. More research is needed into the health problems and health status of migrant and seasonal farmworker families. (*Am J Public Health* 1990; 80:1213–1217.)

Introduction

Migrant farmworker families are believed to experience poor health compared to the general population.[1] However, their health status has not been well measured, and many studies have not been published in peer reviewed journals. As a result, large gaps exist in the data on basic health status indicators in the migrant population. The contributing factors to this poor health status are even less well documented. I undertook a literature review to assess the state of our knowledge on migrant farmworker health.

Methods

MEDLINE files from 1966 through October 1989 were searched, using the subject headings of migrants and transients (US), health, agriculture, and agricultural workers' diseases; all articles relating to US populations containing the title word "migrant" or "farmworker" were also scanned. A total of 485 articles were identified through this search, and 203 were judged after further review to make specific reference to the health of migrants, farmworkers, or farmers in the United States.* The bibliographies of these articles were then scanned to identify any relevant articles missed by the computer search. In addition, I had access to one unpublished literature search undertaken for the Bureau of Health Care Delivery and Assistance (USPHS-DHHS) in 1984,[2] and a second literature search first published by the Farmworker Justice Fund in 1985[3] and revised in 1988.[4] The outcomes of these previous literature searches are dealt with in the discussion section of this paper.

Subject matter was divided into 12 categories, including both adult and pediatric health status, health care utilization patterns, health care delivery systems, and eight specific categories of illness by type of disease or organ system. Articles were also analyzed by year of publication.

Results

Table 1 provides data on the outcome of the search. A further breakdown of the types of articles found by topic and by year of publication (Table 2) illustrates the changing focus of research in migrant health over the past 24 years. The early years were a time of interest in nutritional status, health care delivery systems, and obstacles to health care for the migrant farmworker population. Interest in the risk of pesticides and in the prevalence of infectious diseases showed evidence of continually increasing activity. The first article on AIDS (acquired immunodeficiency syndrome) and HIV (human immunodeficiency virus) seroprevalence in this population appeared in 1987.[5] No articles prior to 1980 dealt with specific psychiatric or behavioral illness patterns, but in the 1980s quantitative studies have begun to appear in the areas of family violence,[6] substance abuse,[7] and specific psychiatric symptomatology.[8]

Topics on which a significant volume of data were found include pesticide risk (including carcinogenic potential), infectious diseases (especially parasites, enteric pathogens, and tuberculosis), and health care delivery. The disciplines of clinical nutrition, dentistry and, to a lesser extent, pediatrics have displayed continuing interest in migrant workers' health.

TABLE 1—Overview of the Medical Literature in Migrant Health, 1966–89

Subject Area	Migrant-Specific Articles	Farm & Farm Labor (general)	Total
Health Status (Adult)	4	3	7
Health Status (Children)	14	—	14
Nutritional Status	10	—	10
Dental Health	18	—	18
Health Care Utilization	9	—	9
Health Care Delivery & Obstacles to Care	43	—	43
Psychiatric or Behavioral Conditions	7	—	7
Cardiovascular Disease	2	—	2
Infectious Disease	17	1	18
Cancer	—	12	12
Pesticides	22	23	45
Occupational Hazards	6	12	18
Total	152	51	203

As early as the 1960s, nutritionists were active in assessing the overall nutritional health status of adults,

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TABLE 2—Subjects of Interest in Migrant Health Literature, by Year of Publication

Subject Area	Year of Publication 1966–73	 1974–81	 1982–89
Health Status (Adult)	2	0	5
Health Status (Children)	4	4	6
Nutritional Status	5	3	2
Dental Health	5	7	6
Health Care Utilization	0	5	4
Health Care Delivery & Obstacles to Care	23	14	6
Psychiatric or Behavioral Conditions	1	1	5
Cardiovascular Disease	2	0	0
Infectious Disease	3	5	10
Cancer	1	2	9
Pesticides	4	17	24
Occupational Hazards	4	5	9
Total	54	63	86

children, and pregnant women in the migrant farmworker population.[9] While under-nutrition (protein-calorie malnutrition, vitamin deficiency, and iron-deficiency anemia) was the focus of previous surveys,[10] future studies will be needed to assess areas of over-nutrition such as obesity and hyperlipidemia.

The dental profession has published many studies assessing the dental health of migrant children and adults using a community-based screening approach.[11]

The results of several community-based, health screenings of migrant children have been published.[12] While most of the studies published in the 1970s screened only for lead poisoning, the 1980s have seen some broader assessments. However, none have been performed on a large scale, with unbiased sampling methods and attention to differences among various ethnic groups as well as between the three US migrant streams. Table 3 lists a variety of basic questions on migrant health to which we find virtually no answers in the peer-reviewed medical literature. These are discussed in the following section.

Discussion

The Missing Denominator—How Many Migrants Are There?

In migrant health we lack even such basic data as crude death rates, median survival, infant and maternal mortality, and incidence of permanent disability. One of the major difficulties in computing these is the lack of a precise denominator. We do not know how many migrants there are, because of the transient nature of the population, their migrations into and out of the US (both randomly and seasonally), undercounting of workers who meet the legal definition of a migrant but do not fit ethnic or demographic stereotypes, and the desire of many immigrant workers (documented or not) to avoid contact with government agencies.

The Office of Migrant Health estimates that there are three million "migrant and seasonal farmworkers and their dependents" in the United States.[13] Estimates of the number of "hired farmworkers" in 1985 from the National Agricultural Statistics Service varied from about 1 million (using one method of counting) to over 2.5 million (using a different method).[14] Their surveys were only able to come up with

TABLE 3—Unanswered Questions in Migrant Health

A. Population Characteristics
  1. Size of the Migrant and Seasonal Farmworker Population
  2. Age Distribution, Ethnicity, and Family Size of Farmworker Families in East, Central, and West Coast Migrant Streams
B. Mortality and Survival Data
  1. Median Survival
  2. Crude Death Rates
  3. Age Distributions (Mortality curve)
  4. Age-Specific Causes of Death
C. Peri-Natal Outcome Data
  1. Birthweight and Prematurity
  2. Neonatal vs Post-Neonatal Infant Mortality*
  3. Fetal wastage (Miscarriage & Stillbirth)
  4. Congenital Anomalies
  5. Maternal Morbidity/Mortality
D. Chronic Diseases
  1. Prevalence of Chronic Diseases
  2. Rates of Hospitalization or Bed-Disability Days
  3. Incidence of Various Types of Cancer
  4. Controllable Medical Risks for Cardiovascular Events
    a) Hypertension
    b) Diabetes
    c) Hyperlipidemia
    d) Smoking
    e) Previous Cardiac Ischemia or Angina
E. Occupational Risks
  1. Annual Highway Mileage (Risk of Motor Vehicle Accident)
  2. Pesticide Exposure (Frequency of Acute Poisonings and Effects of Chronic Low-Level Exposures)
  3. Compliance with Field Sanitation Laws
  4. Accidental Injury (Falls, Farm Machinery, etc.)
  5. Incidence of Occupational Dermatoses by Crop & Chemical Exposure
  6. Effects of Poor Housing
  7. Frequency & Severity of Heat & Cold Exposures
F. Nutritional Factors
  1. Obesity
  2. Serum Cholesterol and Lipid Profiles
  3. Protein/Calorie Malnutrition and Nutritional Anemias in New Migrant Sub-Populations (Haitian and Central American Refugees)
G. Health-Related Behaviors
  1. Tobacco Usage
  2. Alcohol Consumption
  3. Other Substance Abuse
  4. Seat-Belt Use
  5. Risk Factors for AIDS
  6. Suicide/Homicide and Family Violence
H. Accessibility to Health Care
  1. Utilization of Peri-Natal Care
  2. Immunization Status
  3. Treatment of Acute Illness Events (i.e., Strep pharyngitis)
  4. Utilization of Recommended Cancer Screening
  5. Delays in Diagnosis/Treatment Prior to Hospitalization

159,000 "migrant farmworkers" in 1985, a number well below most other estimates.[15]

The Bureau of Labor Statistics asserts that "the size of the hired farm working force declined from an average of 3.6 million in the 1950s to 3.2 million in the 1960s and has been fairly steady at 2.7 million in recent years."[16] The same study notes a decline in the migrant farmworker population from 400,000 in the 1960s to 200,000 in the 1970s.

Several reasons exist for these discrepancies. The first is a question of defining terms. The numbers quoted above do not refer to the same population, but rather to various sub-groups. The Office of Migrant Health's definition is the broadest ("migrant and seasonal farmworkers and their dependents") and therefore gives the largest estimate. The Department of Labor and the Department of Agriculture surveys generally count only employed farmworkers over age 14 (each department using different methodologies).

There are no published estimates of the number of days worked by migrant workers in a typical year, but with the common use of day-laborers the farm labor force may be expected to have a significant number of days without work. Methods such as those used by the Department of Labor that only count "hired farmworkers" at a given point in time may underestimate the true size of the farmworker population. Similarly, the methodology published by the Office of Migrant Health[17] based on crop acreage and the number of person-hours required to harvest a given crop would also be expected to undercount the farmworker population by an amount proportionate to the number of farmworkers unemployed during that harvest season.

In describing a study population it must always be noted whether a given population estimate is referring only to migrant farmworkers, or to migrant and seasonal farmworkers, or to a composite of farmworkers, crew chiefs, and farm managers. The estimate must also be examined for its inclusion or exclusion of family members and dependents, as well as unemployed farmworkers. Characteristics of the overall population will not necessarily be representative of workers in different geographic streams (East, West, and Central), of workers in different seasons (upstream and downstream) or on different crops, or of the various ethnic and other sub-populations of the farmworker population. Current estimates of the migrant population just do not have the needed accuracy or reliability to be used as denominators in the calculation of morbidity and mortality figures.

Mortality Data

In the study period (1966–89) there was no published study which effectively measured median age of survival, crude death rates, or age-specific mortality in the migrant farmworker population. A literature search commissioned by the Department of Health and Human Services in 1984 reviewed over 400 articles in 60 journals and uncovered only "sporadic documentation" of health problems, none of which included specific mortality or survival data.[2] The Farmworker Justice Fund undertook a similar literature review in 1985 and again in 1988 which documented a variety of occupational and lifestyle-associated hazards, but found no hard data on health indicators.[3,4]

Death certificate data in general has limitations,[18] but there are additional problems specific to migrant farmworkers. In no state is migrant status recorded on the death certificate, so deaths of agricultural workers would include seasonal and homebased farmworkers, thus diluting out the specific health effects of migratory lifestyle. Another problem is the "healthy worker effect," the exclusion of former farmworkers who have returned to their country of origin or who have become unemployed or disabled prior to their death. Members of the extended family, including children, who undoubtedly engage in farm labor may or may not be identified as having a primary occupation.

Perinatal Outcomes

A nutritional survey done by Chase, *et al*, in 1971 in Colorado derived from their maternal interviews an estimate of infant mortality among Mexican American farmworkers in Colorado that was nearly three times that of the general population (63 per 1,000).[19] A more recent study (1978) randomly surveyed 145 married women in migrant farmworker households in Wisconsin.[20] Of these, 132 women had given birth to a total of 629 children (excluding stillbirths). The reported infant mortality rate was 29 per 1,000, while early childhood deaths (age 0–5 years) occurred at a rate of 46 per 1,000. Cause of death was not reported. Large-scale maternal interview studies to define infant mortality in the farmworker population have not been undertaken.

Unfortunately, a large sample of perinatal outcome data from migrant health centers has never been analyzed for publication in the peer-reviewed literature. Migrant Health Centers have been estimated to reach approximately 17 percent (500,000) of the estimated 3 million who live in migrant and seasonal farmworker families.[13] Women receiving comprehensive perinatal care in a migrant health center might be expected to have lower infant mortality rates than those who receive no prenatal care prior to hospital delivery or those whose babies are delivered by a traditional birth attendant, but this has never been documented.

Occupational Risks

In 1987 agriculture surpassed mining as the nation's most hazardous occupation with 1,700 work-related deaths (52 per 100,000 workers). The US Bureau of Labor Statistics estimates that there are 12.7 cases of injury and illness per 100 fulltime workers per year.[21] Several reviews of the specific occupational hazards of agricultural labor are available.[3,22] Hazards include chronic and acute pesticide exposures, lack of safe drinking water and toilets, occupational dermatoses, acute injuries (falling from heights and farm machinery injuries), and chronic low-grade back and joint trauma. Most of these risks have been poorly quantified. One study of emergency room visits for farm equipment injuries suggests a methodology for future studies and monitoring of acute agricultural illnesses and injuries.[23]

The difficulty in quantifying pesticide exposures has been documented best in California, which has the nation's strongest mandatory reporting legislation. The state reported a 30 percent reduction in pesticide poisoning from 1985 to 1986, not from an actual reduction in risk but rather from a change in the criteria for documenting exposures.[24] The scant data that have been published on chronic or low-level pesticide exposure, suggest that limb-reduction birth defects,[25] childhood leukemias[26] and brain tumors,[27] adult lymphomas and lymphosarcomas[28] may be linked with occupational exposure to pesticides.

The Council on Scientific Affairs of the American Medical Association recently reviewed findings of the US Environmental Protection Agency and of the International Agency for Research on Cancer with regard to the carcinogenicity of agricultural chemicals. They report two of 53 chemicals to be *definitely* carcinogenic (arsenic and vinyl chloride). In addition they found 13 of 53 to be *probably* carcinogenic, and 16 of 53 *possibly* carcinogenic.[29] Sharp, *et al*, have also published an excellent review of the carcinogenic and neurotoxic effects of chronic low-level exposure to pesticides.[30]

Disability

A 1974 survey found that 44.5 percent of migrant farmworker households had one or more members who described themselves as disabled, but this study did not obtain clinical correlation of the degree or cause of the disability.[31] No survey of workers for the prevalence of disabling musculoskeletal conditions was found in this review.

Infectious Diseases

A recent study of 709 migrant farmworkers on the Delmarva Peninsula showed a high rate (37 percent) of PPD positivity (10 mm or greater) on TB skin testing, but found only one case of active tuberculosis,[32] suggesting that the prevalence of tuberculosis among migrant farmworkers may have been overestimated in previous studies which relied on skin testing. The complete absence of articles on the most common infections seen in clinical practice, such as otitis media or streptococcal pharyngitis in children, was striking. Similarly the most common infectious causes of hospitalization among migrants in this author's experience—such as cellulitis, diabetic foot infections, pneumonia, and appendicitis—all are absent from the literature on migrant health.

Chronic Diseases and Premature Mortality

A basic problem with the predominance of research on conventional topics of migrant health—such as pesticides, TB, and parasites—is that it may give disproportionate attention to diseases that are more common among migrants, but still may not be the major cause of their mortality, e.g., cardiovascular disease and complications of diabetes.

There have been a plethora of health care utilization studies documenting the most common diagnoses among migrants seeking health care.[2] What all these studies tell us is that while some uncommon diseases are more prevalent among migrants, common diseases such as diabetes and hypertension in adults still lead the list. From the current literature base it is impossible to calculate the incidence, prevalence, or risk factors for cancer, heart disease, or stroke in the migrant farmworker population, even though these are the most common causes of death in the US.[33]

Socioeconomic Status

Clearly the migrant population is poor—the average migrant farmworker earned only $3,295 per year (1985) from farm labor, and income from all sources was only $6,194.[34] Few studies compared the health problems of farmworker families to other low-income minority groups rather than to the general population. An example of this more meaningful comparison is one which compared blood levels of migrant children to those of a population of urban poor children.[35]

Conclusions

Some progress has been made. Professionals in dentistry and clinical nutrition have made good baseline assessments of the health status of their clients and are now ready to move into on-going monitoring and intervention programs to improve dental and nutritional health status. In other areas we have only small foci of data, often in stereotyped migrant-specific disease categories. New areas such as psychiatric and behavioral morbidities are beginning to be explored, and methodologies are becoming more precise and quantitative. Such studies will need to be undertaken across a broad range of farmworker sub-populations to determine the extent to which results can be generalized to all farmworkers. Other basic indicators of health and disease, as well as the size of the total population and its sub-sets, remain totally unknown.

While services provided by migrant health centers may have improved the overall health of migrant farmworker families by improving their access to health care, there are very limited data with which to prove this point. Neither can it be proven whether the health problems of migrant farmworkers are the same as those of other groups suffering from poverty and powerlessness, or whether there are migrant farmworker-specific factors in their occupation and lifestyle which contribute to death or disease. The fields of undiscovered knowledge in migrant health are vast and ready for harvest. More research is needed.

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The author is solely responsible for the opinions and conclusions expressed in this article, which do not necessarily reflect the position of the Community Health Centers, Inc., the US Public Health Service, or the Migrant Clinicians' Network.

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IVACG Releases Statement on Role of Vitamin A in Child Health and Survival

The XIII International Vitamin A Consultative Group (IVACG) Meeting in November 1989 reviewed the evidence available to date on the relationship of vitamin A depletion and deficiency to childhood morbidity and mortality. Results from completed studies as well as preliminary findings of others underway were presented and discussed by experts from several disciplines. The IVACG Steering Committee realized the need for an interim statement summarizing the weight of evidence available because results from several large, randomized masked trials are unlikely to be available for one to two years. The following statement, released in June 1990, represents the steering committee's careful consideration of the available evidence.

- An adequate vitamin A status prevents nutritional blindness and contributes significantly to child health and survival.
- The role of vitamin A in preventing nutritional blindness is well documented. Evidence is accumulating that it also reduces mortality. The mechanism(s) by which it has this effect is unclear.
- The impact of improved vitamin A nutrition will vary with the severity of vitamin A deficiency and the contributions of other ecological factors.
- It is therefore imperative to improve the diet and raise the level of vitamin A nutrition where a current intake is inadequate.

The IVACG Steering Committee hopes that this statement will be useful in the process of formulating policies and programs to control and combat vitamin A deficiency. The International Vitamin A Consultative Group was established in 1975 to guide international activities aimed at reducing vitamin A deficiency in the world. For further information, contact the IVACG Secretariat, The Nutrition Foundation, Inc., 1126 Sixteenth Street, NW, Washington, DC 20036. Tel: (202) 659-9024.

Paternal Military Service in Vietnam and the Risk of Late Adverse Pregnancy Outcomes

ANN ASCHENGRAU, SCD, AND RICHARD R. MONSON, MD, SCD

Abstract: To investigate the relationship between paternal military service in Vietnam and the risk of late adverse pregnancy outcomes, we conducted a case-control study of women who delivered infants from August 1977 until March 1980 at Boston Hospital for Women. Paternal military service history among 857 congenital anomaly cases, 61 stillbirth cases, and 48 neonatal death cases were compared with that of 998 normal controls. Military service veterans were identified by crossmatching identifying information from obstetric records with state and national military records. After controlling for confounding variables, we found that the Vietnam veterans' relative risk of fathering an infant with one or more major malformations was 1.7 (95% CI = 0.8, 3.5) compared to non-Vietnam veterans. The increased risk was present in several organ systems and did not seem to be related to a particular type of defect. No associations or highly unstable associations were found between paternal military service in Vietnam and the occurrence of congenital anomalies overall, minor malformations, normal variants, stillbirths, and neonatal deaths. These findings should be viewed with caution since maternal and delivery characteristics appear to have contributed to the etiology of several of the major malformations among the Vietnam veterans' children. (*Am J Public Health* 1990;80:1218–1224.)

Introduction

Many Vietnam war veterans have expressed concern that their children are at increased risk of adverse health effects, particularly congenital anomalies, because of wartime exposure to the herbicide Agent Orange.[1-3] The results of studies published to date suggest that the overall risk of congenital anomalies is not greater among Vietnam veterans but that the risk of specific defects or the risk among specific subgroups may be increased.[4-7] We undertook the present case-control study to investigate the relation between paternal military service in Vietnam and a wide range of late adverse pregnancy outcomes including congenital anomalies, stillbirths, and neonatal deaths.

Methods

Study Population

The present analysis used subjects identified for a prior investigation on maternal risk factors for late adverse pregnancy outcomes.[8-9] In the previous study, we enrolled 14,130 obstetric patients who delivered infants at least 20 weeks' gestation from August 1977 until March 1980 at Boston (Massachusetts) Hospital for Women Division of Brigham and Women's Hospital. This represented 82.5 percent of all delivery patients during the study period; lack of personnel was the main reason for not being enrolled.

For the current study, we selected three case groups and one control group from the enrolled patients. The congenital anomaly case group consisted of 1,314 women who delivered live- or stillborn infants with one or more congenital anomalies. The stillbirth case group consisted of 121 women who delivered stillborn infants without anomalies, and the neonatal death case group was made up of 76 women who delivered infants without anomalies but who died shortly after birth. The 1,490 controls were randomly selected from the remaining women who delivered infants without anomalies who were alive upon discharge to achieve an approximate 1:1 case-control allocation ratio.

The original study interview obtained information on maternal demographic characteristics, medical and obstetric conditions, and habits. In addition, the medical records were reviewed to gather information on the delivery and infant characteristics. For the current study, we re-reviewed the medical records for identifying paternal information not previously obtained and for more detailed information on the pregnancy outcome. For women with stillbirths and neonatal deaths, we obtained the underlying cause of death. For women delivering infants with congenital anomalies, we recorded up to five anomaly diagnoses using a modification of International Classification of Diseases 9th Edition developed by the Centers for Disease Control (CDC) (unpublished coding manual). Anomaly coding decisions followed CDC guidelines and were reviewed for accuracy by a dysmorphologist. In addition, follow-up information was sought from pediatricians and hospitals to confirm the cardiovascular defects. Review of medical records and coding of anomalies were done before military service history was determined.

The medical records of 2,599 women (86.6 percent) were located for re-review. Both cases and controls whose records were lost were more likely to be Black, less educated, and younger than women whose records were reviewed. In addition, 507 women whose records were reviewed were unmarried. Among 84.0 percent of the unmarried women as well as 18 married women, we found no identifying paternal information in their medical records.

In the current study, we excluded women whose records were not located for review, unmarried women, married women without identifying paternal information and women with various diagnoses, and the second pregnancy of those with more than one pregnancy during the study period (see Appendix A for details). This left 857 congenital anomaly cases, 61 stillbirth cases, 48 neonatal death cases, and 998 controls for the final analysis.

Military Service Information

We identified military veterans by crossmatching identifying paternal information from the medical record with: the Massachusetts veterans' bonus list and Massachusetts military records, and the military records at the National Personnel Records Center (NPRC) Military Records Division in St. Louis, Missouri. The identification process and review of

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Massachusetts and NPRC records were performed without knowledge of case or control status of subjects.

Potential Massachusetts veterans were identified by manually searching the bonus list of 250,000 for husbands' names. Potential matches were confirmed by reviewing more complete identifying information in individual military discharge papers. The discharge papers also provided information on the branch, rank, place and dates of service.

Under the Freedom of Information Act, we were able to obtain information on branch, last rank, dates of active service and, if applicable, dates, first rank, and occupational specialty for Vietnam service of all military veterans in our study population. We were denied information on the exact geographic locations of Vietnam service.

In addition to names, Social Security numbers, needed to identify veterans in national records, were obtained from the bonus list for identified Massachusetts veterans and from Massachusetts Registry of Motor Vehicle drivers' license records for the remainder. We located Social Security numbers for 1,641 husbands (83.9% of case husbands and 83.2% of control husbands). Those without numbers were more likely to be Black and born in a foreign country and were included only in the Massachusetts bonus list review.

Analysis

We performed three analyses basing military service history on: 1) the Massachusetts veterans' bonus list alone; 2) national records alone; and 3) both record sources combined. Military service history was categorized as: 1) Vietnam veteran; 2) non-Vietnam veteran; and 3) no known military service.

Husbands were classified as Vietnam veterans if they received a $300 bonus and/or their military records noted the receipt of a Vietnam service medal or listed Vietnam as a place of foreign service. For US Navy personnel, Vietnam veterans were identified by linking individual ship assignments to Naval ship location records. Husbands were classified as non-Vietnam veterans if they received a $200 bonus and/or their military records contained no information on Vietnam service. Husbands were classified as having no known military service if they were not found on the Massachusetts bonus list or if they had no identifiable military records nationally. A national military record was identified but could not be reviewed for four individuals. These husbands were considered veterans with unknown place of service and, when appropriate, were excluded from the analysis.

In the analysis that combined military service information from both Massachusetts and national records, husbands identified as Vietnam veterans in either or both sources were classified as Vietnam veterans. Husbands identified as non-Vietnam veterans in both sources or as a non-Vietnam veteran in one source and as a non-veteran in the other source were classified as non-Vietnam veterans. Husbands were classified as having no known military service if they were classified as such according to both record sources.

To identify Vietnam veterans who might be at increased risk of adverse pregnancy outcomes because of possible exposure to phenoxy herbicides during combat, Vietnam veterans were classified as having probable combat experience on the basis of their branch and occupational specialty by the Director of the Massachusetts Agent Orange Program without knowledge of case or control status of subjects.

We calculated the exposure odds ratio (relative risk) to measure the strength of association between paternal Vietnam service and each type of adverse pregnancy outcome. The odds of each adverse outcome among Vietnam veterans and non-Vietnam veterans was compared to that among men with no known military service. In addition, the odds of each pregnancy outcome among Vietnam veterans were compared to that among non-Vietnam veterans to control for confounding by factors related to entry into military service. Ninety-five percent confidence intervals (CI) for the crude odds ratios were computed using Miettinen's test-based method[10] if there were more than five exposed cases and Fisher's exact method[11] if there were five or fewer exposed cases.

We examined paternal military service history in each case group and then divided the congenital anomaly cases into several subgroups. We categorized anomaly cases according to severity: 1) one or more major malformations; 2) only minor malformations; or 3) only normal variants using a scheme developed by the Metropolitan Atlanta Congenital Defects Program (unpublished procedure manual). Anomalies were also categorized into 13 organ system groups and into specific diagnostic categories. Infants with more than one anomaly diagnosis could contribute to more than one organ system or diagnostic group.

We assessed confounding by entering 44 potential confounding variables into a logistic regression model one at a time and by comparing the adjusted and crude odds ratios[12] (see Appendix B for details). In the regression analyses, the dependent variables included all congenital anomalies, major malformations, minor malformations, and normal variants. Because the number of exposed subjects was small, no adjusted analyses were performed on the stillbirth, neonatal death, and most organ system case groups.

Final logistic regression models were developed for the anomaly cases and severity subgroups that adjusted for several variables simultaneously. The final models included variables that had altered the crude odds ratios by at least 10 percent as well as the following variables of a priori interest: maternal race, educational level, average alcohol consumption during the first trimester, prior infant with a congenital anomaly, and year of pregnancy.

Results

Table 1 displays military service history based on the combined Massachusetts and national data among husbands of cases and controls, and the crude odds ratios of each adverse pregnancy outcome. Compared to men with no known military service, Vietnam veterans, and, to a lesser extent, non-Vietnam veterans had an increased risk of fathering infants with one or more major malformations (ORs = 1.8 and 1.4, respectively). The relative risk of major malformations among Vietnam veterans fell to 1.3 when they were compared to non-Vietnam veterans (95% CI = 0.7, 2.4).

No material increases in the crude relative risks of minor malformations, normal variants, or neonatal deaths were observed among the military service groups. Vietnam veterans had an increased risk of stillbirths but confidence intervals are very wide. The underlying causes of death among stillbirths did not differ among the military service groups.

Most results were similar when military service history was based either on the Massachusetts bonus list or NPRC records alone. However, the relative risks of major malformations and stillbirths fluctuated according to information source. These variations may be accounted for by the small number of exposed cases (data available from author).

Compared to non-veterans, the crude relative risks of defects from several organ systems were elevated both among Vietnam veterans and non-Vietnam veterans (Table 2). The largest increases in risk among Vietnam veterans

TABLE 1—Military Service History, Crude Odds Ratios and 95% Confidence Intervals for All Congenital Anomalies, Congenital Anomaly Severity Subgroups, Stillbirths, and Neonatal Deaths

	Military Service History*			Odds Ratios** Comparing		
	Number of Vietnam Veterans	Number of Non-Vietnam Veterans	Number of Men with No Known Military Service	Vietnam Veterans to Men with No Known Service	Non-Vietnam Veterans to Men with No Known Service	Vietnam Veterans to Non-Vietnam Veterans
All Congenital Anomalies (N = 857)	55	146	656	1.3 (0.9, 1.9)	1.0 (0.8, 1.3)	1.2 (0.8, 1.9)
One or More Major Malformations (N = 214)	18	45	151	1.8 (1.0, 3.1)	1.4 (1.0, 2.0)	1.3 (0.7, 2.4)
Only Minor Malformations (N = 232)	11	32	189	0.9 (0.5, 1.7)	0.8 (0.5, 1.2)	1.1 (0.5, 2.4)
Only Normal Variants (N = 411)	26	69	316	1.2 (0.8–2.0)	1.0 (0.7–1.4)	1.2 (0.7–2.1)
Stillbirths (N = 61)	5	5	51	1.5 (0.4–3.9)	0.5 (0.1–1.2)	3.2 (0.7–14.5)
Neonatal Deaths (N = 48)	3	9	36	1.2 (0.2–4.2)	1.2 (0.6–2.5)	1.1 (0.2–4.5)

*Military service history was based on the combined Massachusetts and NPRC data.

**Odds ratios were computed by comparing paternal military service history of each case group to that of the 995 controls; 52 control husbands were Vietnam veterans, 167 were non-Vietnam veterans, and 776 had no known military service. Three control husbands who were identified as veterans but whose place of service was unknown were excluded.

TABLE 2—Military Service History and Crude Odds Ratios According to Major Malformation Organ System

	Military Service History*			Odds Ratio# Comparing		
Organ System	Number of Vietnam Veterans	Number of Non-Vietnam Veterans	Number of Men with No Known Military Service	Vietnam Veterans to Men with No Known Service	Non-Vietnam Veterans to Men with No Known Service	Vietnam Veterans to Non-Vietnam Veterans
Nervous System (N = 24)	3	3	18	2.5	0.8	3.2
Eye (N = 2)	0	0	2	0.0	0.0	0.0
Ear, Face, Neck (N = 1)	0	0	1	0.0	0.0	0.0
Cardiovascular (N = 27)†	4	7	16	3.7	2.0	1.8
Respiratory (N = 14)	0	4	10	0.0	1.9	0.0
Gastrointestinal (N = 22)	1	4	17	0.9	1.1	0.8
Genital (N = 16)	2	4	10	3.0	1.9	1.6
Urinary Tract (N = 13)	1	4	8	1.9	2.3	0.8
Musculoskeletal (N = 98)	7	21	70	1.5	1.4	1.1
Endocrine (N = 2)	1	1	0	∞	∞	3.2
Autosomal Chromosome Defect (N = 17)	1	3	13	1.2	1.1	1.1
Congenital Syndrome (N = 7)	0	2	5	0.0	1.9	0.0

*Military service history was based on the combined Massachusetts and NPRC data.

#All confidence intervals for the odds ratios include 1.0.

†Cardiovascular defects among infants with Trisomy 21 are excluded.

were for malformations of the nervous system, cardiovascular system, genital organs, and urinary tract.

The organ system results were similar but somewhat attenuated when Vietnam veterans were compared to non-Vietnam veterans. The organ system risk estimates should be interpreted cautiously since they were based on a small number of exposed subjects.

When we examined the specific anomaly diagnoses and clinical notes among the 18 major malformation cases whose husbands served in Vietnam (Appendix C), we found that no one diagnosis predominated within an organ system. In fact, only two defects were observed more than once: two infants had a ventricular septal defect, and three infants had talipes (clubfoot).

Maternal and delivery characteristics appeared to be important contributory factors in the etiology of some malformations. Pediatricians consider that the congenital dislocation of hip and clubfoot were secondary to fetal position; both the mother and prior sibling of the case of adrenal hypoplasia had a history of adrenal insufficiency. None of the medical records of these major malformation cases noted that the husband was a Vietnam veteran.

We also examined military service history among five diagnostic categories of skin and related anomalies: abnormal palmar creases (N = 24), sacral dimples (N = 78), hemangiomas (N = 83), benign neoplasms of the skin (N = 25), and other specified skin anomalies (N = 152). The crude relative risks of abnormal palmar creases and sacral dimples were increased among Vietnam veterans when compared either to non-veterans or non-Vietnam veterans (OR 3.7, 95% CI = 0.8, 12.1 and OR 2.5, 95% CI = 1.2, 5.3, respectively, for the comparison between Vietnam veterans and non-veterans; OR 3.2, 95% CI = 0.6, 17.8 and OR 1.8, 95% CI = 0.8, 4.3, respectively, for the comparison between Vietnam veterans and non-Vietnam veterans). The remaining categories of skin anomalies were not materially elevated among Vietnam veterans nor were any skin anomalies materially increased among non-Vietnam veterans. Because normal variants like abnormal palmar creases can be markers for more serious defects, we reanalyzed these data excluding infants with major malformations. Upon reanalysis, the relative risks of palmar creases and sacral dimples among Vietnam veterans remained elevated.

In Table 3 we have presented the military service characteristics of Vietnam veteran case and control husbands. A greater proportion of congenital anomaly and major malformation case husbands versus control husbands served in the Marine Corps and had longer durations of Vietnam service. Anomaly case husbands were also more likely to have enlisted and have had initial occupational specialties in Vietnam likely to involve combat.

Because Vietnam veterans who were in combat had a greater likelihood for herbicide exposure than veterans who were not,[13] we recalculated the odds ratios for all congenital anomalies and the severity subgroups considering as exposed only Vietnam veterans with probable combat experience. Compared to non-Vietnam veterans, the relative risks of congenital anomalies overall, one or more major malformations, only minor malformations, and only normal variants among Vietnam veterans with likely combat exposure were similar to those risks among all Vietnam veterans (1.4, 1.1, 1.4, and 1.5, respectively). The number of Vietnam veterans with probable combat exposure among the stillbirth and neonatal death case groups was too small to permit meaningful analysis.

Many available characteristics of the study population were potential confounders because of their association with paternal military service history and a particular pregnancy outcome. When we adjusted simultaneously for confounding variables using logistic regression models, we found that the relative risk of one or more major malformations rose to 2.2 for the comparison between Vietnam veterans and non-veterans (crude OR 1.8) and to 1.7 for the comparison between Vietnam veterans and non-Vietnam veterans (crude OR 1.3) (Table 4). The adjusted relative risks for congenital anomalies overall and the other severity subgroups differed little from the crude relative risks. Confidence intervals are again very wide.

Discussion

In our study population, we have observed positive associations between paternal military service in Vietnam and the risk of fathering an infant with one or more major malformations even after controlling for available confounding variables. The increased risk was present in several organ systems and did not seem to be related to a particular type of defect. We also found positive associations between two normal variants of the skin and Vietnam service. No associations or highly unstable associations were observed between Vietnam service and congenital anomalies overall, minor malformations, normal variants, stillbirths, and neonatal deaths.

The positive findings warrant cautious interpretation since maternal and delivery characteristics appeared to be important factors in the etiology of the endocrine and some of the musculoskeletal malformations observed among the children of the Vietnam veterans. In addition, most risk estimates for the organ systems were unstable because they were based on a small number of subjects.

One might also argue that cautious interpretation is needed because of the wide variety of major malformations seen among the Vietnam veterans' children. However, the etiologic implications of the lack of a predominant defect or discernible pattern of defects are unclear, because so little is known about the possible biologic mechanisms by which paternal exposures might influence pregnancy outcomes and because many well-known maternal exposures have been associated with a wide range of defects (e.g. maternal prenatal ingestion of thalidomide has been associated with limb, ear, eye, heart, gastrointestinal tract, and genital organ defects).[14]

TABLE 3—Distribution (%) of Paternal Military Service[*] Characteristics among Vietnam Veterans According to Outcome

Characteristics[**]	Congenital Anomaly Cases (N = 55)	1+ Major Malformation Cases (N = 18)	Still-Birth Cases (N = 5)	Neonatal Death Cases (N = 3)	Controls (N = 52)
Military Branch					
Army	49.1	50.0	60.0	66.7	50.0
Navy	18.2	16.7	40.0	0.0	25.0
Air Force	10.9	11.1	0.0	33.3	15.4
Marines	21.8	22.2	0.0	0.0	9.6
Year Started Vietnam Service					
1964–1966	8.2	7.6	20.0	0.0	10.2
1967–1969	71.4	61.5	40.0	100.0	61.2
1970–1972	20.4	30.8	40.0	0.0	28.6
Duration of Vietnam Service (months)					
1–6	18.8	8.3	20.0	0.0	25.5
7–12	56.3	58.3	40.0	100.0	59.6
13–27	25.0	33.4	40.0	0.0	14.9
First Rank in Vietnam					
Enlisted	83.6	77.8	80.0	66.6	76.9
Officer	16.4	22.2	20.0	33.3	23.1
Probable Combat Exposure	56.4	44.4	20.0	66.7	50.0

[*] Military service history was based on the combined Massachusetts and NPRC data.
[**] Individuals with unknown values were excluded.

TABLE 4—Adjusted Odds Ratios and 95% Confidence Intervals for Late Adverse Pregnancy Outcomes According to Military Service History

	Adjusted Odds Ratio	95% Confidence Interval
Vietnam Veterans Compared to Non-Veterans		
All Congenital Anomalies	1.2*	0.8, 1.8
1+ Major Malformations	2.2**	1.2, 4.0
Only Minor Malformations	0.7***	0.3, 1.5
Only Normal Variants	1.1*	0.7, 1.9
Stillbirths	1.5‡	0.6, 3.8
Neonatal Deaths	1.2‡	0.4, 4.2
Non-Vietnam Veterans Compared to Non-Veterans		
All Congenital Anomalies	1.1*	0.8, 1.4
1+ Major Malformations	1.4*	0.9, 2.2
Only Minor Malformations	0.7†	0.5, 1.2
Only Normal Variants	1.1*	0.8, 1.5
Stillbirths	0.5‡	0.2, 1.1
Neonatal Deaths	1.2‡	0.6, 2.5
Vietnam Veterans Compared to Non-Vietnam Veterans		
All Congenital Anomalies	1.1*	0.7, 1.8
1+ Major Malformations	1.7††	0.8, 3.5
Only Minor Malformations	0.9†††	0.4, 2.3
Only Normal Variants	1.0*	0.6, 1.8
Stillbirths	3.2‡	0.7, 14.5
Neonatal Deaths	1.1‡	0.2, 4.5

*Adjusted for maternal race, educational level, alcohol use during the first trimester, history of another child with an anomaly, year of pregnancy.

**Adjusted for maternal race, educational level, alcohol use during the first trimester, history of another child with an anomaly, year of pregnancy, and parity.

***Adjusted for maternal race, educational level, alcohol use during the first trimester, history of another child with an anomaly, year of pregnancy, and employment status at delivery.

†Adjusted for maternal race, educational level, alcohol use during the first trimester, history of another child with an anomaly, year of pregnancy, and prenatal urinary tract infection.

††Adjusted for maternal race, educational level, alcohol use during the first trimester, history of another child with an anomaly, year of pregnancy, prior use of an intrauterine contraceptive device, and month prenatal care began.

†††Adjusted for maternal race, educational level, alcohol use during the first trimester, history of another child with an anomaly, year of pregnancy, employment status at delivery, prenatal urinary tract infection, DES exposure, and cigarette and marijuana smoking during pregnancy.

‡Unadjusted results.

In the current investigation, congenital anomaly diagnoses were made usually within a few days of birth by pediatric residents who were not specialists in teratology. Thus, it is quite likely that some anomalies were missed. We believe that this misclassification was not related to military service history and so probably biased some results towards the null.

We believe it is unlikely that the positive association observed for major malformations was due to more complete ascertainment of these congenital anomalies among the children of Vietnam veterans. Anecdotal reports of adverse reproductive outcomes among Vietnam veterans potentially exposed to Agent Orange began appearing in the medical literature in late 1979 after most of the study pregnancies had occurred.[1–3] Most of these malformations had very noticeable cosmetic or medical effects and many were life threatening. Thus, it is unlikely that the diagnosis or notation of a defect would be affected by the father's military service history. Furthermore, none of the medical records of the major malformation cases noted that the husband was a Vietnam veteran.

We also regard it as unlikely that these results simply reflect a differential tendency for Vietnam veteran versus non-Vietnam or non-veteran cases and controls to have participated in the original study. For practical reasons, enrollment in the current study was limited to married women whose records contained identifying paternal information. Enrolled women were predominantly White and college educated while the excluded women were more likely to be Black and less educated. Because the demographic characteristics of both excluded cases and controls were similar, it is unlikely that these differences led to bias. However, generalizations from this study should be limited to veterans who are demographically similar to the enrolled population.

Observation bias was improbable because identification of veterans was done blindly using military records. To control potential confounding, we excluded high-risk women and, when possible, used multivariate techniques to adjust for other variables. In addition, we compared Vietnam veterans to other veterans in order to control for factors related to entry into military service. However, since we lacked specific data on paternal exposures and conditions, it is possible that confounding was not completely controlled.

Studies have been conducted among North Vietnamese military veterans who were possibly exposed during the Vietnam war.[15,16] Positive associations were generally found but their validity is difficult to assess since they have never been published but have only been described briefly by scientists who attended the 1983 International Symposium on the Effects of Phenoxy Herbicides.

In contrast, two case-control studies conducted among Australian Army and US Vietnam veterans found no overall increase in the risk of major malformations (ORs 1.03 and 0.97, respectively).[4,5] The Centers for Disease Control study found that US Vietnam veterans with greater estimated opportunities for Agent Orange exposure had stable increases in the risk of fathering infants with spina bifida (but not anencephaly), cleft lip with or without cleft palate, congenital neoplasms, and coloboma.[5] The Australian study found that Army veterans had unstable increases in the risk of fathering children with ventricular septal defects and Down's Syndrome.[4]

Preliminary results from a retrospective cohort study among the US Air Force personnel who conducted the aerial herbicide spraying missions in Vietnam revealed an elevation in the risk of fathering infants with major and minor birth defects combined (OR: 1.3) that was due primarily to minor skin anomalies. Unlike our study, the skin anomalies reported among the Air Force children were mainly birthmarks and other skin discolorations. Investigators also observed no increase in the risk of stillbirths but a 3.8-fold increase in the risk of neonatal deaths. Recall bias cannot be ruled out in the Air Force data since they were based solely on interviews; collection of birth records to verify these associations is currently underway.[6]

Another US study further examined reproductive and other health outcomes among a cohort of Army veterans. At interview Vietnam veterans were more likely to report that they fathered a child with a birth defect than were non-Vietnam veterans (OR: 1.3, 95% CI:1.2, 1.4). In contrast, a sub-study using only diagnoses recorded in hospital records found similar rates of major, minor and "suspected" birth defects among Vietnam and non-Vietnam veterans (OR's: 1.1, 1.0, 0.9, respectively).[7]

In summary, current and previous study results are not in agreement concerning the risk of major malformations among Vietnam veterans. No consistent pattern of defects has emerged. We conclude that large studies, preferably with individual herbicide exposure data, would be needed to clarify the risk of late adverse pregnancy outcomes among Vietnam veterans overall as well as the subgroup of veterans who were exposed to Agent Orange.

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APPENDIX A

Selection of Cases and Controls for Study of Paternal Vietnam Service and the Occurrence of Late Adverse Pregnancy Outcomes

	Number of Congenital Anomaly Cases	Number of Stillbirth Cases	Number of Neonatal Death Cases	Number of Controls
Selected	1,314	121	76	1,490
Medical Record Reviewed*	1,159	87	66	1,287
Exclusions:				
Unmarried woman**	253	20	14	238
Diabetes	29	4	—	27
Epilepsy	4	3	2	7
Drug Abuse	6	—	—	—
Herpes, Toxoplasmosis, Rubella Infection	10	—	2	12
Second Pregnancy During Study Period	16	—	1	15
Total Number Excluded***	302	26	18	289
Total Number in Vietnam Service Study	857	61	48	998

*These figures also reflect changes in outcome status after record review and follow-up.

**Unmarried women are single, separated, divorced, or widowed. In addition, 18 married subjects whose husbands' names were not recorded in the medical record were excluded here.

***Since some subjects fell into more than one exclusion category, the total number of women excluded is less than the sum of women in each exclusion category.

APPENDIX B

Potential Confounding Variables Considered in Analysis

Paternal age
Maternal age
Paternal educational level
Maternal educational level
Paternal race
Maternal race
Paternal birthplace
Maternal birthplace
Paternal employment status at delivery
Maternal employment status at delivery
Medical insurance
Religion
Maternal history of prior oral contraceptive use
Maternal history of prior IUD use
Intent to become pregnant
Trimester prenatal care started
Maternal history of hypertension
Maternal history of cervical incompetence
Maternal history of pelvic inflammatory disease
Maternal history of gonorrhea
Maternal history of DES exposure
Maternal history of gynecologic surgery
Maternal history of other chronic medical conditions
Prenatal pre-eclampsia
Prenatal hypertension
Prenatal urinary tract infection
Gravidity
Parity
Number of prior livebirths
Number of prior pregnancy losses
Number of prior induced abortions
Number of prior ectopic pregnancies
Maternal history of cigarette smoking
Average number of cigarettes smoked per day during first trimester
Maternal history of alcohol intake
Average number of alcoholic drinks consumed per week during first trimester
Maternal marijuana use during pregnancy
Maternal coffee consumption during first trimester
Maternal tea consumption during first trimester
Maternal use of nausea medication during pregnancy
Maternal use of prescription drugs during first trimester
Family history of a prior malformed child
Gender of infant
Calendar year of pregnancy

APPENDIX C

Congenital Anomaly Diagnoses among Major Malformation Cases Whose Husbands Served in Vietnam

Case Number	*Anomaly Diagnoses Coded* (Relevant Clinical Notes)
1	Congenital hydrocephalus (secondary to intraventricular hemorrhage)
2+	Reduction deformity of brain, cleft palate without cleft lip, perineal hypospadias
3	Encephalocele, rockerbottom feet*
4	Probable ventricular septal defect (too early to tell for certain, murmur, tachypnea, tachycardia, acrocyanosis)
5	Ventricular septal defect, undescended testes,* flame nevi*
6+	Patent ductus arteriosus, patent foramen ovale, simian crease* (congestive heart failure, intracranial hemorrhage, pulmonary artery hypertension)
7	Transposition of the great vessels
8	Congenital dislocation of the hip (breech presentation)
9	Talipes equinovarus (severe tibial torsion)
10	Talipes equinovarus
11	Talipes calcaneovalgus (secondary to fetal position)
12	Hypoplasia of mandible and zygomatic bone
13	Arthrogryposis (30° contracture of elbows, 15° contracture of knees)
14	Split hand deformity
15	Congenital hydronephrosis
16	Ovarian cysts
17	Congenital adrenal hypoplasia (adrenal insufficiency in mother and sibling)
18	Trisomy 21 (membraneous ventricular septal defect)

*These diagnoses were classified as minor malformations or normal variants.
+Died

Lyme Disease in New Jersey Outdoor Workers: A Statewide Survey of Seroprevalence and Tick Exposure

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Abstract: To evaluate the spread of Lyme disease in New Jersey, we conducted a statewide cross-sectional study of Lyme disease seroprevalence in a high-risk occupational group of outdoor employees. Of the 689 employees who participated in the study, 39 (5.7 percent) were positive for antibody to *B. burgdorferi*, the causative agent of Lyme disease. Seroprevalence varied markedly by county; unexpectedly high seroprevalence rates were found in several northern counties (Sussex, Hudson, and Hunterdon). Furthermore, some southern counties (Atlantic, Cape May, and Ocean) with large tick populations (as measured by self-reported exposure to ticks) had low seroprevalence rates which were inversely correlated with self-reported preventive practices. These data suggest that lyme disease, as measured by seroprevalence of antibody to *B. burgdorferi*, may be spreading beyond the southern portion of the state where it had been previously well documented and that preventive behaviors may play an important role in minimizing the risk of the disease. (*Am J Public Health* 1990; 80:1225–1229.)

Introduction

The incidence of Lyme disease is increasing in many areas of the United States. The disease is caused by the spirochete *Borrelia burgdorferi* and transmitted by the *Ixodid* ticks. Early reports of the disease in the United States were from Connecticut in the late 1970s[1] but the disease is now a public health concern in the surrounding states (New Jersey, New York, and Massachusetts) as well, and has been reported in at least 43 states.[2]

A series of investigations in New Jersey were performed during the period 1978–82 by Bowen and Schulze, *et al.*[3–7] They found that, of 117 reported Lyme disease cases during the period, 48 percent (57) had occurred in one centrally located county (Monmouth). Almost all cases (98 percent) had occurred in the central and southern portions of the state.[5] Furthermore, the statewide distribution of *Ixodes dammini* correlated with the location of reported cases and revealed a high density of *Ixodes dammini* in the southern two-thirds of the state and a particularly high concentration in Monmouth County. It should be noted that while *Ixodes dammini* is the primary vector of Lyme disease in the northeast United States, the causative agent, *B. burgdorferi* has been identified in a number of species of ticks including *Amblyomma americanum*, and *Dermacentor variabilis*.[8]

In an attempt to further evaluate the spread of Lyme disease in New Jersey, we conducted a statewide cross-sectional study of Lyme disease seroprevalence in a high-risk occupational group. We measured: 1) seroprevalence of antibody to *B. burgdorferi*, 2) self-reported tick exposure and, 3) self-reported preventive practices among outdoor workers in the Natural and Historic Resources divisions of the New Jersey Department of Environmental Protection.

Methods

Study Population

The New Jersey Natural and Historic Resources (NHR) Section consists of four divisions: Parks and Forestry; Coastal Resources; Green Acres; and Fish, Game and Wildlife. Employees work primarily in outdoor jobs in a variety of habitats including mountainous regions, grass lands, forests, and shoreline. Geographically, they are distributed across the state from Stokes State Forest on the state line with New York in the north to Cape May County across the bay from Delaware in the south. During October 1988, we conducted a Lyme disease evaluation of employees at 12 different sites across the state on 15 dates. The summer months of May through August are the highest risk months and antibody seroconversion generally occurs three to six weeks after infection.[9] Participation was voluntary and all participating employees gave informed consent. A total of 689 (69 percent) of an estimated 1,000 eligible employees participated in the study.

Data Collection

The evaluation consisted of venipuncture for a serum specimen and administration of a questionnaire. Whole blood specimens were centrifuged and then divided into as many as five equal aliquots. An initial fresh specimen was sent to a commercial laboratory for immunofluorescent antibody (IFA) titer to *B. burgdorferi*. A titer of 1:128 or greater was reported as positive by the laboratory. The remaining samples were frozen and then after the initial fresh specimen results were reported, all positives and a random sample of the negatives were sent to as many as three other laboratories for analysis. Samples were analyzed at one department of health laboratory and at two university research laboratories by IFA in one case and enzyme linked immunosorbent assay (ELISA) in the other two. To be defined as positive for antibody to *Borrelia burgdorferi* in the study, the worker had to have at least two positive tests in two independent laboratories.

All employees participating in the study completed a self-administered questionnaire. The administration of the questionnaire was supervised by the authors and checked for accuracy after completion. Study variables included demographic data, counties of work and residence, self-reported measures of tick exposure, and frequency of performance of six behavioral practices of potential benefit in minimizing the risk of *B. burgdorferi* infection.

For purposes of data analysis and description, the counties of the state have been defined as northern or southern based on a line which cuts New Jersey geographically in half. The line runs from the lower border of Mercer

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County through the middle of Monmouth County (Figure 1). Since the dividing line runs through Monmouth County, and because that county is unique in that it has a particularly well documented history of elevated Lyme disease risk, Monmouth will be discussed separately and not included with the northern or southern groupings.

Results

Seroprevalence

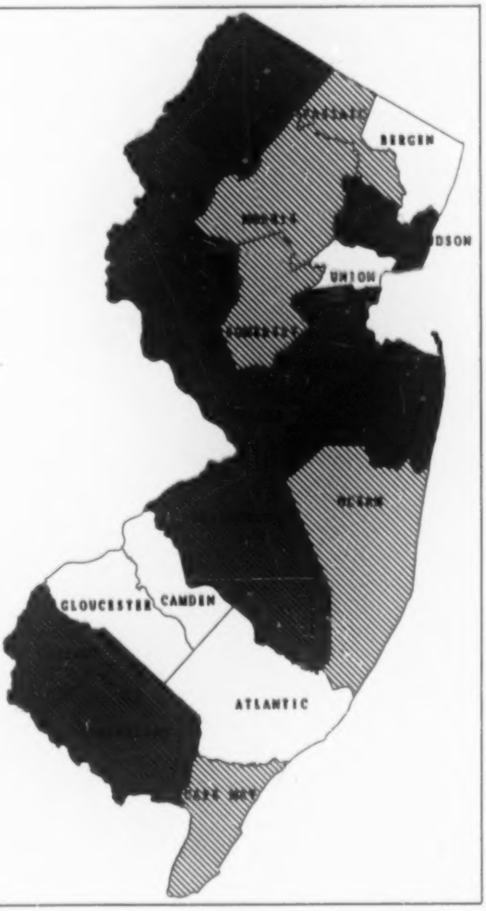
Statewide: A total of 689 employees of the NHR divisions of the NJ Department of Environmental Protection participated in the study. Thirty-nine employees (5.7 percent) had at least two positive tests for antibody to *B. burgdorferi*, the causative agent of Lyme disease. There were no differences in seropositivity based on years of outdoor state employment. The 39 seropositive subjects were found to have a mean (SD) of 16.5 (28.9) years of outdoor state employment while the seronegatives had a mean (SD) of 19.0 (28.0) years. There were no important differences based on job title or primary job habitat.

Geographic Distribution: Figure 1 displays the distribution of seropositives based upon county(s) of employment (some employees worked in more than one county on a regular basis). Seroprevalence ranged from a low of zero percent in four counties (Bergen, Camden, Gloucester, and Union) to highs of 6.5, 7.2, 7.8, and 18.5 percent in Hunterdon, Sussex, Monmouth, and Hudson counties, respectively. The 20 percent seroprevalence found in Essex County is based upon only five workers sampled.

Self-Reported Tick Exposure

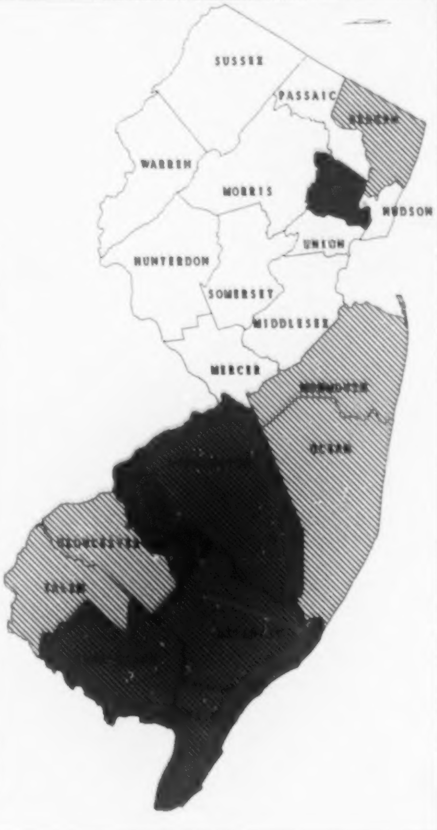
Statewide: Based on self-reports from the 689 employees who participated in the study, the workers reported a mean (SD) of 3.5 (7.6) and a median of 1.0 tick bites (ticks embedded in the skin) during the past year. The number of ticks removed from skin or clothing per week (during May–August 1988) on the primary job (some employees had other non-DEP jobs) was reported as a mean of 2.5 (SD ± 5.4) and a median of 2.0

Geographic Distribution: Figure 2 displays the mean number of tick bites over the past 12 months by county of employment. The mean yearly bite totals ranged from less than 1.5 in Hudson, Sussex, Union, and Warren counties to greater than 7.5 in Essex, Cumberland, and Camden counties. The mean number of ticks removed from skin or clothing per week on the primary state job by county of employment ranged from less than 1.5 ticks per week in Bergen, Passaic, Sussex, and Union counties to greater than 4.0 ticks per week in Burlington, Cape May, Cumberland, and Salem counties.



COUNTY	NUMBER SEROP.	NUMBER SAMPLED	PERCENT SEROP.
ATLANTIC	1	117	0.90
BERGEN	0	20	0.00
BURLINGTON	6	134	4.50
CAMDEN	0	24	0.00
CAPE MAY	1	61	1.60
CUMBERLAND	2	55	3.60
ESSEX	1	5	20.00
GLOUCESTER	0	12	0.00
HUDSON	5	27	18.50
HUNTERDON	5	77	6.50
MERCER	5	110	4.50
MIDDLESEX	2	40	5.00
MONMOUTH	10	129	7.80
MORRIS	1	52	1.90
OCEAN	5	141	3.50
PASSAIC	1	57	1.80
SALEM	1	21	4.80
SOMERSET	1	32	3.10
SUSSEX	9	125	7.20
UNION	0	2	0.00
WARREN	4	83	4.80

FIGURE 1—Percent Seropositive by County of Employment



COUNTY	BITES PER YEAR
ATLANTIC	6.7
BERGEN	3.5
BURLINGTON	6.8
CAMDEN	11.6
CAPE MAY	6.7
CUMBERLAND	7.8
ESSEX	12.0
GLOUCESTER	6.0
HUDSON	1.0
HUNTERDON	2.0
MERCER	2.4
MIDDLESEX	2.3
MONMOUTH	3.2
MORRIS	2.4
OCEAN	4.2
PASSAIC	2.1
SALEM	3.3
SOMERSET	2.6
SUSSEX	1.0
UNION	1.0
WARREN	1.3

FIGURE 2—Mean Number of Self-reported Tick Bites per Year by County of Employment

Preventive Measures: Self-reported behavioral practices are displayed in Table 1 on a statewide basis and by selected counties in Table 2. These behaviors were performed more frequently on the job than in non-occupational settings. Additionally, although workers frequently checked themselves for ticks, a minority of workers reported the other behaviors. In an effort to account for the unexpectedly high seroprevalence rates found in three northern counties (Sussex, Hudson, and Hunterdon) we chose to compare the preventive behavior performance frequencies in these counties with the frequencies found in three southern counties with relatively low seroprevalence rates. Table 2 reveals that these preventive behaviors were performed more frequently by employees in Monmouth County and three selected southern counties (Atlantic, Ocean, and Cape May) than they were in the three northern counties (Sussex, Hudson, and Hunterdon). The results for the other northern and southern counties were similar to those for the selected northern and southern counties reported.

TABLE 1—Percent of Workers Who Report Performance of Preventive Behaviors Statewide

	Percent Who Perform Behavior While Outdoors		
Specific Behavior	Frequently (Usually or Always)	Sometimes	Never
Wear long pants in the summer			
At work	85.7	10.7	4.3
Not at work	47.9	44.3	7.7
Wear long sleeves in the summer			
At work	13.7	37.8	48.5
Not at work	6.7	48.7	44.6
Tuck pants into socks or shoes			
At work	8.2	21.4	71.0
Not at work	3.6	17.3	79.2
Use insect repellent on skin			
At work	22.6	47.0	30.6
Not at work	17.7	50.4	31.8
Use insect repellent on clothes			
At work	19.3	43.2	37.5
Not at work	16.2	44.6	39.1
Check self for ticks			
At work	74.9	14.4	10.7
Not at work	65.9	22.8	11.3

Discussion

To our knowledge, the present study is the first to investigate the seroprevalence of antibody to *B. burgdorferi* on a statewide basis.

Several studies have investigated the seroprevalence or the seroconversion rate of populations residing or working in endemic areas. An early investigation in 1982 reported a one-year clinical Lyme disease cumulative incidence rate of

1.1 percent in 1,364 residents and employees living on or around the grounds of Naval Weapons Station Earle in Monmouth County, New Jersey.[10] A 1984 study of 176 residents of a Fire Island, New York summer community revealed that 9.7 percent had serological evidence of exposure to the Lyme spirochete in the initial cross-sectional portion of the study.[11] A 1986 study of long-term residents on Great Island, Massachusetts reported a seroprevalence of 8 percent among 121 asymptomatic residents.[12] More recently, an evaluation of 190 residents living within 5 kilometers of a nature preserve in Ipswich, Massachusetts from 1980–87 revealed a Lyme disease attack rate of 35 percent based on a clinical case definition.[13] Seventy-three percent of those with clinical disease and 23 percent of all residents tested were found to be seropositive for *Borrelia burgdorferi*-specific antibody. A 1982 comparison of outdoor versus indoor workers at Naval Weapons Station Earle revealed a five-fold higher cumulative incidence rate for Lyme disease among outdoor workers.[3] Finally, a recent study by Smith, *et al*, of 414 outdoor workers in southeastern New York State revealed a Lyme disease seroprevalence of 6.5 percent among these employees.[14] This was 5.9 times higher than the seroprevalence of a comparison group of anonymous blood donors from the same region.

It should be noted that participation in the study was voluntary and therefore unequal participation by county is a potential source of bias. Rates of participation on a county-by-county basis were not possible to determine. We did, however, find that the main determinant of participation was whether or not the employee's primary work location was one of the screening sites. These sites included an equal number of randomly distributed northern and southern locations. Job duties were similar in all the counties and the vast majority of all subjects statewide had not previously been tested. Therefore we feel it is unlikely that there was any specific county characteristic which resulted in a differential degree of study participation.

Our statewide seroprevalence of antibody to *B. burgdorferi* (5.7 percent) in a high-risk group of outdoor workers is comparable to the 6.5 percent seroprevalence found by Smith, *et al*, in New York State. When examined on a county-by-county basis, however, there were some unexpected findings. Earlier studies by Bowen and Schulze of Lyme disease distribution in New Jersey (1978–82) had reported a large number of case reports, as well as a high density of *Ixodes dammini*, in Monmouth County and the southern half of the state. Their results revealed a paucity of cases and ticks in the northern half of the state.[3–7] The present study revealed that one of five counties with seroprevalences greater than the statewide mean of 5.7 percent was Monmouth County and the others—Sussex, Hunterdon, Hudson, and Essex—were all counties in the northern half of the state (Figure 1). The Essex finding can be discounted because of a very small denominator (n = 5) but denominators for the other counties were much larger (n = 27 to 129). Similar (unpublished) analyses of distribution based on county of residence revealed seven counties with seroprevalence rates greater than the statewide mean. One was Monmouth, but again five of the remaining six (Sussex, Hudson, Middlesex, Somerset, and Mercer) were in the northern half of the state.

The preponderance of northern counties with elevated seroprevalence was not matched by an increased level of self-reported tick exposure in these counties. In fact, as displayed in Figure 2, the vast majority of counties with tick exposures greater than the statewide mean were southern counties; for "total tick bites in the past year," seven out of eight were southern counties. Similarly for "ticks removed from skin or clothing per week on primary job," eight out of 10 were southern counties.

In three southern counties, where seroprevalence was low but tick exposure was high, the employees performed the preventive measures on a "frequent" basis more often than their colleagues statewide (based on mean results from all 689 employees). In Monmouth County, the traditional hotbed of Lyme disease in New Jersey where only a moderately elevated seroprevalence rate was found, the employees also reported performance of preventive measures at a greater frequency than the statewide mean. Finally in three northern counties with relatively high seroprevalence rates and relatively low tick exposure, the employees were performing preventive measures less frequently than other employees statewide.

These findings suggest that the performance of preventive behaviors may reduce the risk of exposure to *B. burgdorferi*. These results do not establish a causal relationship but do merit further investigation. It may be postulated that there has been a relatively recent spread of infected ticks to the northern counties and, although their numbers are still not great, the northern ticks are feeding on a more susceptible human population.[13] The well-publicized history of Lyme disease in the southern counties may have led to a better educated public in these counties and therefore a greater awareness of ticks and appropriate risk reduction behaviors. It is possible that a certain number of individuals from southern counties where Lyme disease had been better publicized responded with expected behavior rather than

TABLE 2—Percent of Workers Reporting Frequent Preventive Behavior Performance for Selected New Jersey Counties

	Specific Behaviors					
County	Long Sleeves (13.7)*	Tuck Pants (8.2)*	Skin Repellent (22.3)*	Clothing Repellent (19.3)*	Tick Check (74.9)*	Number of Behaviors Greater than Statewide Mean
Atlantic	14.0	15.6	32.5	34.2	86.9	5/5
Ocean	16.8	12.4	29.2	27.7	89.0	5/5
Cape May	13.1	16.6	42.6	41.0	93.4	4/5
Monmouth	17.5	10.4	27.8	27.8	84.9	5/5
Sussex	13.4	4.2	10.9	9.2	53.8	0/5
Hudson	7.6	11.5	22.0	11.5	69.2	1/5
Hunterdon	10.7	2.7	10.7	8.0	78.6	1/5

*Statewide mean percent for frequent performance (usually or always) actual behavior leading to a potential source of bias. This differential Lyme disease awareness may have also resulted in an overreporting of tick exposure in the southern counties and a relative underreporting in the northern counties. A comprehensive statewide study of tick concentrations would help to resolve this last possibility. However, some limited statewide data (Schulze TL: unpublished data) suggest that tick concentrations are much lower in the northern part of the state and that differential reporting of tick exposure is, in fact, not likely to be the explanation for the observed differences in seroprevalence.

In summary, the findings suggest that Lyme disease, as measured by seroprevalence of antibody to *B. burgdorferi*, appears to be spreading beyond Monmouth County and southern portions of the state where it had been previously identified. This spread into the northern counties may not necessarily be solely from southern New Jersey but could also reflect the spread of disease from bordering Orange and Rockland counties in New York. Unexpectedly high seroprevalences were found in several northern New Jersey counties (Sussex, Hudson, and Hunterdon). These high seroprevalence rates in regions of relatively low tick exposure, coupled with low rates (Atlantic, Ocean, and Cape May) and surprisingly moderate rates (Monmouth) in areas of higher tick exposure may be related to preventive behaviors. These results suggest that simple preventive behaviors may have a significant impact on minimizing the risk of Lyme disease.

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Evaluating the Impact of Municipal Water Fluoridation on the Aquatic Environment

JOHN W. OSTERMAN, MD, SCD

Abstract: Although highly beneficial for dental health, low concentrations of fluoride in environmental waters may be toxic to several organisms. In an era of heightened public awareness about the environment, this may lead city officials to withhold implementing water fluoridation for environmental reasons. This paper presents a mass balance approach to evaluate this perceived risk. Generally speaking, fluoridated water loss during use, dilution of sewage by rain and ground water infiltrate, fluoride removal during secondary sewage treatment, and diffusion dynamics at effluent outfall combine to eliminate fluoridation-related environmental effects. In Montreal, water fluoridation would raise average aquatic fluoride levels in the waste water plume immediately below effluent outfall by only 0.05–0.09 mg/l. Downstream, these changes would be only 0.02–0.05 mg/l at 1 km, and 0.01–0.03 mg/l at 2 km below outfall. Overall river fluoride concentrations theoretically would be raised by 0.001–0.002 mg/l, a value not measurable by current analytical techniques. All resulting concentrations would be well below those recommended for environmental safety and would not exceed natural levels found elsewhere in Quebec. A literature review did not reveal any examples of municipal water fluoridation causing recommended environmental concentrations to be exceeded, although excesses occurred in several cases of severe industrial water pollution. (*Am J Public Health* 1990; 80:1230–1235.)

Introduction

The beneficial effects of water fluoridation for human health are widely recognized.[1–3] Optimally fluoridated drinking water significantly reduces dental caries in both children and adults.[2–5] Fluoride may also reduce the incidence of osteoporosis and hip fractures, although the evidence is controversial.[6–8] No side effects occur.[1–3] Although the prevalence of mild dental fluorosis may increase, the esthetic effects of this mild tooth whitening are greatly outweighed by the improved esthetics of fewer decayed, missing, and filled teeth.[9] By far the most cost-effective intervention in dentistry,[10] optimally fluoridated water is provided in more than 10,000 North American communities and in countries around the globe.[11–13]

The toxic environmental effects of fluorides are also well documented, however. Airborne fluoride pollution from industrial sources may cause severe effects in plants by inhibiting photosynthesis, chlorophyll production and carbohydrate metabolism, with resulting defoliation or death.[14–16] Most plants accumulate fluoride which may lead to bony and dental fluorosis, lameness, arthritis, and other symptoms in wild and domestic herbivores foraging downwind from fluoride air pollution sources.[17]

As a water pollutant, elevated concentrations of fluoride may affect a number of organisms, including fish, amphibians, insects, snails, shellfish, protozoa, and some aquatic plants.[18] Fresh water fish, especially rainbow trout and other trout species, appear to be particularly sensitive and may show growth and behavioral changes, decreased survival, and prolonged hatching time when exposed to moderate levels.[19] Under negligible water hardness conditions, lethal effects for rainbow trout may occur at fluoride concentrations as low as 2.7–4.7 mg/l[20] and one undocumented observation reported delayed hatching of trout eggs at 1.5 mg/l.[21] Small amounts of calcium carbonate found in soft or moderately hard water, however, greatly reduce these effects,[22] as do water hardness generally, alkalinity, the presence of metallic ions (particularly calcium and magnesium) and chloride.[22–24] Toxicity increases with water temperature, by increasing fish metabolism.[25]

To protect aquatic organisms, several authorities recommend an upper limit between 1.0 mg/l and 1.8 mg/l of fluoride for fresh water systems.[18,26–28] Others feel that the environmental literature on fluoride toxicity is incomplete. They recommend that levels protecting drinking water (generally 1.2 to 2.0 mg/l) also be used to protect the environment, arguing that detectable effects occur in humans at lower concentrations than in other species.[29–32] Nevertheless, some states allow concentrations as high as 5–10 mg/l if the contaminated water is not subsequently used for human consumption.[33] No effluent standards exist.

Industrial waste and municipal sewage may add to the fluoride which is naturally present in all surface water.[33] In an era of heightened public awareness about environmental issues, concerns of public interest groups may lead city officials and politicians to withhold water fluoridation for environmental reasons, as occurred in Montreal in 1988.

To evaluate the environmental impact of water fluoridation, this paper uses a mass balance (material balance) approach to develop a series of mathematical equations which describe the fate of fluoride added to drinking water in a typical municipal water management system. In this approach, the ionic mass of fluoride entering the aquatic system from all sources is calculated, its distribution followed, and its fate examined; by balancing fluoride inputs and outputs, intervening concentrations and changes may be determined. This approach, widely used in environmental impact analyses,[34] is analagous to the study of physiologic or pharmacologic agents in living organisms.

The equations described below may be applied to readily available data from relevent water authorities to predict potential fluoridation-related changes in environmental waters receiving municipal effluent. These changes may be compared to natural variations in local ambient fluoride concentrations, the scientific literature concerning fluoride toxicity to aquatic organisms, and to recommendations from

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scientific and government agencies. The city of Montreal is presented as an example.

Methods

Fate of Fluorides in Municipal Water Systems

For most municipal water management systems, drinking water is drawn from a lake, river, or subterrain well and is pumped to a purification plant. There it may undergo aeration, flocculation, coagulation and sedimentation, filtration and be disinfected with ozone or chlorine dioxide. Usually a small amount of residual chlorine is maintained in the drinking water to avoid bacterial regrowth in the distribution system. Ambient fluoride concentrations are generally measured in the final stages of water purification. Fluoride is then added to obtain optimal levels, between 0.7 and 1.2 mg/l depending on climatic conditions. Although several fluoride-containing compounds may be used, all dissociate on admixing, thereby liberating free fluoride ion ($F-$).[35] Occasionally, when drinking water sources contain high concentrations of fluoride, the water may be "defluoridated" to optimal levels by one of several methods.[36]

Drinking water is distributed to a variety of residential, industrial, commercial, and municipal clients. Waste water from all these sources is collected by the city sewer system and is transported to the sewage treatment plant. Industrial and human wastes increase sewage fluoride levels. Some fluoride is lost, however, when drinking water is used to water gardens, wash cars, fill pools, extinguish fires, etc. Infiltrating ground water, underground streams, and rain may add to sewage flow and cause considerable dilution.

Primary sewage treatment removes suspended solids and phosphates by screening, filtration, flocculation, coagulation and sedimentation. Several common processes using iron salt coagulation, lime, or activated alumina may remove fluoride at high concentrations; however, these effects are minor at the low concentrations of fluoride found in municipal sewage.[36,37] After initial treatment, waste water undergoes secondary (biological) treatment in order to destroy unwanted organisms and reduce nitrogen levels and biochemical oxygen demand (BOD). The microorganisms present in most secondary treatment systems absorb large quantities of fluoride and may reduce fluoride concentrations in effluent by up to 50 percent.[38,39] Effluent may then undergo further disinfection with chlorine before discharge.

Effluent is generally discharged from an outfall pipe at a lake, river, or ocean bottom. The warmer effluent rises quickly to the surface creating physical turbulence and an immediate dilution which may be as high as 5–15 times. If natural dilution is low, a diffusion apparatus may be installed at effluent outfall which distributes effluent evenly over a wide area to ensure similar dilution levels.[40] Natural currents then carry the waste water downstream, creating a waste water "plume" and secondary dilution over several miles.

Mathematical Equations Evaluating Fluoridation Impact

From this overview of the fate of fluorides used in water fluoridation, mathematical equations may be derived to estimate the impact of fluoridation on the aquatic environment downstream of municipal sewage outfall. Terms used in these equations are defined in Table 1.

Global Impact

An estimate of global environmental impact may be obtained by comparing the fluoride needed to optimally fluoridate drinking water to the amount naturally present in the aquatic system receiving municipal effluent. Adjusted fluoride equals the difference between optimal and pre-existing drinking water fluoride concentrations (ΔF_M) multiplied by the rate per unit time of drinking water production (Q_M). Environmental fluoride equals the sum of fluoride naturally present in drinking water ($F_{M1}Q_M$) and fluoride naturally present in the waters receiving municipal effluent ($F_{E1}Q_E$). Thus,

TABLE 1—Definition of Symbols

*Fluoride Concentrations**
F_M = fluoride concentration in municipal drinking water
F_R = fluoride concentration in raw sewage
F_T = fluoride concentration in treated sewage
F_E = fluoride concentration in environmental water receiving municipal effluent
F_X = fluoride concentration in waste water plume at point X, downstream from effluent outfall site
Flow Rates
Q_M = flow rate (production) of municipal drinking water
Q_S = flow rate of sewage at treatment plant
Q_E = flow rate of environmental water receiving municipal effluent
Portions
P_M = portion of municipal drinking water destined for sewers
P_D = portion of sewage originating as drinking water
PE_X = portion of environmental water affected by waste water plume at point X
Diffusion Factor
DF_X = a unitless number describing cumulative dilution occurring in the waste water plume from effluent outfall to point X downstream

*Fluoride concentrations before and after fluoridation (see text) are respectively indicated by subscripts 1 and 2.

$$\frac{\text{Municipal F}}{\text{Environmental F}} = \frac{\Delta F_M Q_M}{F_{E1}Q_E + F_{M1}Q_M} \tag{1}$$

If Q_M is very small relative to Q_E, in the case of a small municipality discharging into a large river, then Equation 1 simplifies to:

$$\frac{\text{Municipal F}}{\text{Environmental F}} = \frac{\Delta F_M Q_M}{F_{E1}Q_E} \tag{2}$$

Multiple municipalities and river systems may be considered in an additive fashion using the general formula:

$$\frac{\text{Municipal F}}{\text{Environmental F}} = \frac{\Sigma_i \Delta F_{Mi} Q_{Mi}}{\Sigma_i F_{E1i}Q_{Ei} + \Sigma_i F_{M1i}Q_{Mi}} \tag{3}$$

The change in environmental fluoride concentrations due to fluoridation (ΔF_E) may be obtained by dividing the fluoride added to drinking water by the sum of municipal and receiving water flow rates.

$$\Delta F_E = \frac{\Delta F_M Q_M}{Q_E + Q_M} \tag{4}$$

In a multiple city or river situation, this relationship becomes:

$$\Delta F_E = \frac{\Sigma_i \Delta F_{Mi} Q_{Mi}}{\Sigma_i Q_{Ei} + \Sigma_i Q_{Mi}} \tag{5}$$

Obviously, the post-fluoridation concentration in water downstream from municipal sewage outfall equals the sum of the calculated change and the pre-existing concentration. The ratio of these two values ($\Delta F_E/F_{E1}$) is identical to Equation 1.

While conceptually simple, these models overestimate the real effects of fluoridation on the environment by assuming that all drinking water is discharged as waste, by excluding the effects of sewage treatment, and by discounting eventual fluoride deposition into sediments. Moreover, estimates from these models are valid only at some theoretical point downstream where municipal effluent and receiving waters have become thoroughly mixed.

The first of these objections may be overcome by including in the numerator of Equations 1–5 only the percentage of drinking water which is eventually discharged as effluent (P_M). Thus, for example, Equation 1 would be corrected to:

$$\frac{\text{Municipal F}}{\text{Environmental F}} = \frac{\Delta F_M Q_M P_M}{F_{E1}Q_E + F_{M1}Q_M} \qquad (6)$$

Local Impact

To estimate fluoridation-related changes in fluoride concentrations in the waste water plume downstream from municipal effluent outfall, the effect of sewage treatment must first be evaluated by comparing fluoride concentrations in treated (F_{T1}) and raw (F_{R1}) sewage. The ratio of these values (F_{T1}/F_{R1}) shows the portion of fluoride remaining after sewage treatment and is not affected by fluoridation status.[38,39] The concentration of fluoride in post-fluoridation treated municipal effluent (F_{T2}) may then be estimated.

$$F_{T2} = F_{T1} + \frac{\Delta F_M P_D F_{T1}}{F_{R1}} \qquad (7)$$

P_D is the portion of sewage originating as drinking water and equals $Q_M P_M/Q_S$. From the rate of diffusion of waste water in the effluent plume (DF_X), the concentration of fluoride in the plume (F_{X2}) may now be estimated at outfall and for points downstream.

$$F_{X2} = \frac{F_{T2} + F_{E1}(DF_X - 1)}{DF_X} \qquad (8)$$

The change in fluoride concentration at any point downstream from outfall (ΔF_X) equals:

$$\Delta F_X = \frac{\Delta F_T}{DF_X} \qquad (9)$$

Waste water is unequally distributed in the plume. Thus, diffusion, and DF_X, is greatest at the edge where effluent concentrations are least and, conversely, least at the center where concentrations are highest. Also, turbulence may create eddies of poorly diluted effluent at the outfall site, which disappear downstream. It should be noted that DF_X has a maximum value equal to flow in the receiving water (Q_E) divided by flow of municipal sewage (Q_S); generally this limit is important only when large volumes of effluent are discharged into small bodies of water.

The effluent plume affects only a portion of the receiving waters. This portion (P_X) at point "X" may be calculated as follows:

$$P_X = \frac{Q_S(DF_X)}{Q_E} \qquad (10)$$

Results

An Example: The City of Montreal

Montreal's drinking water, serving 1,6 million people, is drawn from the St. Lawrence River, near the Lachine Rapids slightly upstream from the city, and is returned some 35 km downstream at Ile-aux-Vaches. From data provided by municipal, provincial, and federal agencies,[41–47] potential global changes in fluoride levels related to water fluoridation were estimated (Table 2). At the Lachine Rapids the daily water flow of the St. Lawrence averages 883 (range 659–1028) million cubic meters, and natural fluoride levels average 0.13 (range 0.11–0.17) mg/l. On average, therefore, 115 tonnes (tonne = 1000 kg = 2,204.6 pounds) of naturally present fluoride (theoretical range 73–175) flow past Montreal daily. Assuming all municipal drinking water eventually returns to the river, fluoridation would add an additional 1.93 tonnes to this water, or 1/60 (1.7 percent) of naturally occurring amounts. On average, however, only 57 percent of Montreal's drinking water returns to the river, making the additional fluoride load closer to 1.09 tonnes, or 1 percent of natural amounts. This additional charge is well within natural variations in fluoride concentration (±15 percent), river flow (± 16 percent), and fluoride ion mass (±37 percent). Overall, the average concentration of fluoride in the river downstream from effluent outfall would increase by 0.001–0.002 mg/l, a value which is not measurable by current analytical methods.

Excluding rain, Montreal produces an average of 2.4 million cubic meters of sewage per day, of which 42 percent originates as unfluoridated drinking water, 2 percent as fluoridated drinking water from neighboring suburbs, and 56 percent from infiltrating ground water. This latter value is very high, due to Montreal's island geography, and an old combined sewer system in one sector. Optimal fluoridation in Montreal would increase drinking water fluoride concentrations from 0.11–0.15 mg/l to 1.2 mg/l which would in turn increase the average concentration of fluoride in Montreal sewage by 0.45 ± 0.01 mg/l. Daily fluoride concentrations in

TABLE 2—Average Daily Water Flow and Fluoride Levels in the St. Lawrence River and Montreal Water Supplies, before and after Fluoridation (range in parentheses)

	Flow Rate ($m^3 \times 10^6$)	Fluoride Ion Concentration (mg/l)	Fluoride Ion Mass (metric tons)
St. Lawrence River	883 (659–1028)	0.13 (0.11–0.17)	115 (73–175)
Water supply before fluoridation	1.8 (1.5–2.2)	0.13 (0.11–0.15)	0.23 (0.16–0.33)
Water supply after fluoridation	1.8 (1.5–2.2)	1.2	2.16 (1.80–2.64)
Fluoride added to water supply	1.8 (1.5–2.2)	1.07 (1.05–1.09)	1.93 (1.64–2.31)
Fluoride added to waste water from water supply	1.02*	1.07 (1.05–1.09)	1.09 (1.02–1.11)

*Range not available

Montreal sewage average 0.34 ± 0.07 mg/l (mean ± SD) and range from 0.22 to 0.58 mg/l.[45] Thus, after fluoridation, concentrations in Montreal sewage would become 0.79 ± 0.08 mg/l (mean ± SD) and range from 0.66 to 1.04 mg/l. Because Montreal sewage does not undergo biological treatment, little or no fluoride removal occurs at the sewage treatment plant.

The diffusion of Montreal's waste water in the St. Lawrence river was measured in 1983 as part of a feasibility study for the new municipal sewage treatment plant.[46] At sewage outfall a minimum initial diffusion factor of 5 occurred at the center of the waste water plume, and initial diffusion averaged 15 over the plume's entire cross-sectional area. After adjusting for current modifications which will increase outfall capacity and thereby decrease diffusion slightly, an average increase of 0.05 mg/l in fluoride concentration would be predicted across the plume immediately below effluent outfall (Table 3) and an average increase of 0.09 mg/l at the plume's center (Table 4). The plume's average concentration immediately below outfall would be 0.20 mg/l and the average level in the plume center at outfall would be 0.26 mg/l. Given known variations of fluoride ion concentrations in Montreal's sewage, the greatest daily average concentration expected would 0.34 mg/l at the outfall center. These values would decrease rapidly downstream. At 1 km from outfall an increase of only 0.02–0.05 mg/l would be expected. The predicted change at 2 km would be only 0.01–0.03 mg/l and would affect only 3.5–6.3 percent of the river.

Discussion

Using a mass balance approach, mathematical equations may be derived to evaluate the environmental impact of fluoride added to optimally fluoridate municipal water supplies. Generally, it will be shown that fluoridation has little impact on the surrounding aquatic environment. Some fluoride is lost when drinking water is used to water lawns, fill pools, etc; this usually ends up in the soil which may already contain large amounts (100–300 ppm).[3,33] Although fluoride concentrations in the sewer system may increase with the addition of industrial and human wastes, they are diluted by rain and infiltrated ground water. Up to 50 percent of fluoride may be removed during secondary sewage treatment. Initial diffusion rapidly dilutes the remainder at the effluent outfall site. Secondary diffusion causes further reductions downstream. Eventually, the remaining fluoride is incorporated into river sediments, or carried to the ocean which already contain large amounts (1.2–1.4 mg/l).[33] Any toxicity from this residual fluoride would be severely inhibited by other substances present in surface and waste waters, notably water hardness, calcium ion, and chloride.[22–24]

TABLE 3—Estimated Average Daily Fluoride Concentrations (mg/l) across Effluent Plume before and after Municipal Water Fluoridation in Montreal (range in parentheses)

Distance from Outfall (km)	Diffusion Factor*	Concentration before Fluoridation	Concentration after Fluoridation	Change	Portion of River Affected %
0.3	10	0.15 (0.12–0.21)	0.20 (0.16–0.26)	0.05	2.0
1	19	0.14 (0.12–0.19)	0.16 (0.14–0.22)	0.02	3.9
2	31	0.14 (0.11–0.18)	0.15 (0.13–0.20)	0.01	6.3

*Adjusted for current modifications to increase effluent capacity.

TABLE 4—Estimated Average Daily Fluoride Concentrations (mg/l) at Effluent Plume Center before and after Municipal Water Fluoridation in Montreal (range in parentheses)

Distance from Outfall (km)	Diffusion Factor*	Concentration before Fluoridation	Concentration after Fluoridation	Change	Portion of River Affected %
0.3	5	0.17 (0.13–0.25)	0.26 (0.22–0.34)	0.09	1.0
1	10	0.15 (0.12–0.21)	0.20 (0.16–0.26)	0.05	2.0
2	17	0.14 (0.12–0.19)	0.17 (0.14–0.22)	0.03	3.5

*Adjusted for current modifications to increase effluent capacity.

Montreal is a typical example. Due to its island geography, infiltrating ground water in the sewer system is probably greater than elsewhere, but this effect is offset by the lack of a secondary sewage treatment plant. Water fluoridation in Montreal would result in a slight increase in the fluoride concentration of the waste water plume directly below the effluent outfall. These changes would return to pre-existing levels within two kilometers. Global changes would not be measurable. Rain water, not included in this analysis, would reduce sewage concentrations and these findings even further.

The maximum predicted daily concentration at the center of the outfall site (0.34 mg/l) would be well below recommended levels for environmental safety,[18,26–32] and would be similar to natural levels occurring elsewhere. A survey in Quebec showed that average daily fresh water fluoride levels across the province varied from 0.07 to 0.24 mg/l and maximum levels of 1.7 mg/l occurred.[47] The average concentration in US rivers measured at 343 stations of the National Stream Quality Accounting Network in 1975 was 0.33 mg/l[48]; six streams in the southwest US had concentrations of 1.4 to 1.8 mg/l. Other investigators report that fluoride concentrations in US rivers average 0.2 mg/l and range from 0.0 to 6.5 mg/l.[49] In a polluted section of the Illinois River around Peoria, fluoride concentrations averaged 1.08 mg/l and ranged from 0.17 to 2.06 mg/l.[50] The source of the pollution was unspecified. Ocean concentrations range from 1.2 to 1.4 mg/l.[33] One result is that marine and estuarine organisms are relatively immune to the toxic effect of fluoride.[33,51]

The predicted increase of 0.45 mg/l in the fluoride concentration of Montreal sewage due to water fluoridation is similar to findings elsewhere. Fluoride levels in raw sewage from seven fluoridated Ontario communities contained 0.47 mg/l more fluoride than raw sewage from 11 non-fluoridated communities (0.96 vs 0.49 mg/l), and treated sewage differed by 0.33 mg/l (0.62 vs 0.29 mg/l).[38] For 56 California cities, raw and primary treated sewage from fluoridated communities contained an average of 1.80 mg/l (range 1.4–3.2) or 0.37 mg/l more fluoride than non-fluoridated communities (average 1.43; range 0.6–3.6 mg/l).[39] Both studies showed the important effects of secondary sewage treatment which reduced effluent fluoride concentrations by 35 percent in Ontario and by 56 percent in California in both fluoridated and non-fluoridated communities. In California, domestic waste accounted for far more sewage fluoride than water fluoridation.

The fate of fluoride in waste water from municipal and industrial sources has been evaluated by a number of researchers. In 1973, fluoridated Bozeman, Montana (population 20,000) discharged an average of 8.5 m^3/min of primary treated municipal effluent into the East Gallatin River (average flow: 146.7m^3/min). This raised average fluoride levels from 0.33 mg/l, nine meters above outfall, to 0.62 mg/l at 0.3 km downstream.[52] A maximum level of 2.0 mg/l was recorded. Natural fluoride levels were reestablished 5.3 km downstream. Another study at the same site found that fluoride concentrations quadrupled at effluent outfall but returned to natural levels 4 km downstream.[53] These changes were not considered to have any effect on the environment.[29]

In 1977, fluoridated Minneapolis-St. Paul produced effluent at the rate of 9.6 m^3/sec with a fluoride concentration of 1.21 mg/l, which was added to the Mississippi River (flow rate 279 m^3/sec). Water collected 10 air miles below outfall contained the same fluoride concentration as that collected upstream from the sewage disposal plant.[54]

In 1986, Kudo, *et al*,[55] evaluated fluoride concentrations along four small rivers in an industrialized area of the French Alps near unfluoridated Grenoble. This city (population 350,000) added about 1.8 tonnes of fluoride daily in untreated sewage to the Isere River (flow rate 300 m^3/sec) which increased fluoride concentrations from 0.19 mg/l above the city to 0.26 mg/l some 70 km downstream. This study underlined the importance of industrial water pollution sources. On the small Arc River (flow rate 50 m^3/sec) fluoride concentrations increased from 0.13 mg/l to 0.62 mg/l over a 50 km portion during which it received industrial effluents from three aluminum factories, a factory producing silica, and a factory producing phosphates. Severe fluoride-containing air pollution from these companies had destroyed much of the area's vegetation.

In another study underlining the importance of industrial water pollution, Martin and Salvadori[56] found that industrial effluents from a fluorophosphate fertilizer plant in Rouen, France increased fluoride concentrations in the Seine River from 0.25 to 2.0 mg/l which eventually fell to 0.47 mg/l many miles downstream. Fluoride discharge was estimated to be 37 tonnes per day, a quantity which would fluoridate a city 20 times the size of Montreal!

In conclusion, by using a mass balance approach, fluoridation-related changes in environmental concentrations of fluoride may be estimated from knowledge of municipal water management systems and data which are usually readily available from appropriate water authorities. Generally speaking, these changes will be minimal and, except when accompanied by serious industrial pollution, will remain below toxic levels recorded in the literature and recommendations by scientific authorities for the protection of the environment and human health.

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Crop Duster Aviation Mechanics: High Risk for Pesticide Poisoning

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Abstract: A cross-sectional medical survey was conducted among 63 Nicaraguan aviation mechanics exposed to organophosphate and other toxic pesticides. Thirty-one (49 percent) reported having been acutely poisoned on the job. Also, seven of 14 novice mechanics, with less than one year on the job, reported that they had been poisoned. Thirty-eight (61 percent) had cholinesterase levels below the lower limit of normal, including three workers with levels less than 20 percent of the lower limit of normal. Risk factors for low cholinesterase included recent hire and recent poisoning. Workers did not use protective equipment, nor were there facilities for bathing on site. As a result of this survey, the government has prohibited the mixing and loading of pesticides at this airport and requires the washing of planes prior to maintenance work; coveralls and thin, pesticide impermeable gloves are to be issued to mechanics handling pesticide-contaminated parts. Closed system mixing and loading systems have been installed at satellite airstrips. (*Am J Public Health* 1990; 80:1236–1239.)

Introduction

Pesticide poisoning has been a major public health problem in Nicaragua for the last 30 years.[1] The country's principal traditional export is cotton, a crop which is sprayed up to 35 times a season with organophosphate insecticides for control of the boll weevil. Most of this spraying is done from crop dusting airplanes, and poisoning of highly exposed mixers and loaders at the airports and landing strips which service these airplanes has been recognized as a problem, both in Nicaragua and in the developed countries.[2]

The airplane mechanics who service these airplanes are a little studied population who have high exposure to pesticide-contaminated parts. To characterize exposure of these workers to pesticides and to assess any acute health effects, we evaluated mechanics at Nicaragua's largest crop dusting airport in late December 1987.

Methods

The 28 crop dusters owned by the six companies operating out of the airport made approximately 10 flights daily during the peak cotton spraying season (October 15 through early January). It was estimated that as much as 130,000 gallons were sprayed daily on flights originating from this airport, accounting for almost 30 percent of all pesticides sprayed in the department of Chinandega, the principal cotton growing region (Mario Pais, Ministry of Industry, personal communication). The mechanics were under pressure to do minor service and adjustment as quickly as possible, because the companies and pilots were reimbursed for each flight. There was little time to wash planes before minor maintenance. Most exposure was to the hands, since the manipulation of small mechanical parts was necessary for the routine work of changing pesticide filters and adjusting spray nozzles, and difficult to perform while wearing clumsy protective gloves.

The mechanics often did not know what pesticide was loaded in the plane they were servicing. One employee from each company, with responsibility for recording the pesticide used in each flight, characterized frequency of spraying as daily or as less frequently for the various pesticides used at the airport during the month prior to the study.

The 71 mechanics (all men) employed at the airport were invited for a questionnaire interview which asked about history of use of personal protective equipment, history of training regarding poisoning prevention, about previous poisoning, and about symptoms compatible with cholinesterase inhibitors (organophosphate and carbamate insecticides). The questionnaire asked about specific symptoms, such as headache, lightheadedness, blurred vision, lack of appetite, vomiting, stomach ache, and frequent spitting (sialorrhea). Erythrocyte cholinesterase is inhibited by organophosphate insecticides and is an early indicator of overexposure. It was measured using the Ellman assay (adapted for use with a new battery operated field kit), as previously described[3]:

> Briefly, 5 μl of blood was pipetted into a cuvette containing 200 μl of sample buffer containing Tris-HCl, Triton X-100 surfactant, and trace azide. Two ml of reagent solution containing acetylthiocholine iodide substrate, DTNB [5,5'-dithiobis(2-nitrobenzoic acid)] indicator, quinidine sulfate (to inhibit plasma cholinesterase), and phosphate buffer were added to the cuvette. The solution was incubated for three minutes and the change in absorbance noted between one minute and three minutes. The activity was adjusted for temperature and converted to international units. The results were not adjusted for hemoglobin. Forty-six healthy, unexposed male Nicaraguan health workers were sampled in order to establish a lower normal limit of 3.7 international units/minute/ml of blood. (This is the mean minus 1.65 standard deviations).
>
> Each worker was given the result of his cholinesterase assay at the time of the test.
>
> Confidence intervals for relative risk of low cholinesterase for various risk factors were calculated using the test-based method of Miettinen.[4] Multivariate analysis of mean cholinesterase was done using SPSS-PC.[5]

Results

All pesticides sprayed at the airport during the month prior to the survey are listed in the Appendix. Methamidophos, mephosfolan, methyl and diethyl parathion are all US Environmental Protection Agency (EPA) category I (acutely toxic) organophosphate insecticides. Chlorpyrifos (category II) and acephate (category III) are less toxic organophosphates. Cholinesterase depression reflects overexposure to these insecticides. Unfortunately, there are no good field methods for evaluating exposure to the non-

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organophosphate pesticides, although there are several pesticides with chronic effects. A metabolite of chlordimeform was recently reported to be associated with a 73-fold excess risk of bladder cancer in exposed workers.[6]

Questionnaire

Sixty-three mechanics (88 percent) of the 71 who worked at the airport came to the health screening. Those who did not participate had been assigned temporarily to smaller satellite airports, were sick, or refused to participate. This is a relatively mature work force with an average of almost 10 years in the current job (Table 1). Nevertheless, there was a sizable proportion of novices (22 percent) with less than one year of experience, including one 11-year-old and one other worker under age 16, the minimum legal age for work with pesticides.[7] Almost half the workers reported having required medical attention for acute symptoms resulting from pesticide exposure at some time during work at the airport. Twelve (19 percent) of 63 reported that they were poisoned in the previous 12 months, and half of the 14 workers with less than one year of experience had been poisoned. Some older workers reported having been poisoned as many as seven times at the airport. The most common protective equipment used were boots (used by 14 percent), followed by coveralls (11 percent). No worker used protective gloves, a respirator, or protective glasses.

Cholinesterase Measurements

Thirty-eight (61 percent) of the 62 workers sampled had low erythrocyte cholinesterase levels (Table 1). The mean cholinesterase (3.1 international units [IU]/minute/ml blood) for all mechanics was less than the lower limit of normal of 3.7 IU. The lowest level recorded was 0.61 IU, one of three samples less than 20 percent of the lower limit of normal. That worker complained of headache and nausea, had pinpoint pupils and sialorrhea, and was diaphoretic, all of which responded to treatment with atropine sulfate.

We evaluated the following risk factors for depressed cholinesterase levels among these workers: recent poisoning, recent hire, no training about safe use of pesticides, less than daily change of clean work clothes, and symptoms compatible with organophosphate insecticide poisoning. In addition, the mean cholinesterase for workers with each risk factor was compared with the mean for all workers without the risk. Almost all workers poisoned in the previous year and almost all mechanics hired within the previous year had low cholinesterase values at the time of the screening (see Table 2). The presence or absence of more than two symptoms compatible with organophosphate insecticide poisoning was not reflected either in higher prevalence of low cholinesterase values (52 percent compared with 67 percent among those with two symptoms or less) or in lower mean cholinesterase levels.

TABLE 1—Demographic Characteristics, History of Poisoning, and Cholinesterase Levels among Aviation Mechanics, Chinandega, Nicaragua, December 1987 (N = 63*)

Mean age (SD)	29.1 (10.1)
Mean duration (years) of employment (SD)	9.6 (8.2)
Number employed less than 1 year (%)	14 (22)
Number poisoned during employment at airport (%)	31 (49)
Number poisoned in previous 12 months (%)	12 (19)
Number poisoned in previous 12 months among mechanics with less than 1 year employment (%)	7/14 (50)
Number who have received pesticide safety training on current job (%)	16 (26)
Number with low erythrocyte cholinesterase (%)	38 (61)
Mean cholinesterase in international units/minute/ml blood (SD)	3.1 (1.3)

*Because of missing data the denominator varies slightly within this and subsequent tables.

Paradoxically, there was a higher prevalence of low cholinesterase among mechanics who reported a daily change of clean work clothes (87 percent) compared with mechanics who changed work clothes less often (53 percent).

There was a slightly lower prevalence of low cholinesterase levels among workers who had received some previous training about the safe handling of pesticides, and the mean cholinesterase level among workers who had received training (3.6 IU) was higher than among workers without any training (2.9 IU). However, this beneficial effect of training was confounded by the high exposure tasks of recently hired workers, who were also less likely to have received training. After controlling for a dummy variable representing recent hire (within the last year) in a multiple regression procedure, there was still a slight beneficial average effect on cholinesterase of having received training, but the effect was reduced (regression coefficient = 0.41 I.U.; 95% CI = −0.28, 1.13).

Discussion

To our knowledge mechanics engaged in routine maintenance of crop dusters have not been studied previously. At this airport, they were at extraordinarily high risk for pesticide overexposure and for poisoning. Many of these workers reported being hospitalized for treatment, almost exclusively with signs and symptoms compatible with the cholinesterase inhibitors used at the airport. The high prevalence of cholinesterase depression is probably underestimated, because pre-exposure baseline levels of cholinesterase were not available. We therefore used a normal range based on inter-individual variability in cholinesterase. A more appropriate criterion for a low cholinesterase level is a drop of 30 percent from baseline, as recommended by the World Health Organization[8] and the US National Institute for Occupational Safety and Health.[9] Because the inter-individual normal range is almost a two-fold increase over the lower limit of normal, a decrease of well over 30 percent for someone with a high baseline cholinesterase level would still leave that person in the normal range in this study.

In workers with daily exposure to organophosphate pesticides, cholinesterase may be depressed without clinical signs and symptoms of poisoning.[10] The absence of association between symptoms and cholinesterase depression probably reflects the importance of the rate of decline in cholinesterase in producing symptoms.[2] A gradual inhibition of cholinesterase from continued low level exposure to organophosphates is less likely to produce symptoms than the same inhibition from a single large exposure. Our experience is not dissimilar to that reported in other studies, where symptoms sometimes have been found to be associated with chronic depression of cholinesterase and sometimes have not.[2,11–13]

It is likely that experienced workers tolerate the hazards of this job, because it is highly skilled and it pays well. In addition, the most hazardous work is done by the newly hired apprentice mechanics, many of whom do not return the following season. The anomalous increase in proportion of workers with low cholinesterase levels among those who changed to clean work clothes daily probably occurred because these young workers are in the dirtiest, most highly

TABLE 2—Mean Cholinesterase and Frequency of Low Cholinesterase among Aviation Mechanics by Selected Risk Factors, Chinandega, Nicaragua, December 1987

Risk Factor	Number with Low Cholinesterase (%)	Relative Risk (95% CI)	Mean Cholinesterase	Difference of Means (95% CI)
Poisoned in the previous year (N = 12)	11 (92)	1.7 (1.1, 2.6)	1.5 IU	−2.0 (−1.3, −2.7)
Not poisoned in the previous year (N = 50)	27 (54)		3.5 IU	
Less than 1 year in job (N = 14)	13 (93)	1.8 (1.2, 2.7)	2.0 IU	−1.4 (−0.7, −2.1)
One or more year in job (N = 48)	25 (52)		3.4 IU	
Has not received pesticide safety training at airport (N = 45)	30 (67)	1.5 (0.91, 2.5)	2.9 IU	−0.7 (−0.07, −1.3)
Has received training (N = 16)	7 (44)		3.6 IU	
Changes work clothes less often than daily (N = 47)	25 (53)	0.61 (0.40, 0.93)	3.2 IU	0.6 (1.3, −0.1)
Changes work clothes daily (N = 15)	13 (87)		2.6 IU	
More than 2 symptoms compatible with cholinesterase inhibitors (N = 23)	12 (52)	0.78 (0.50, 1.2)	3.0 IU	−0.1 (0.6, −0.8)
Two or fewer symptoms compatible with cholinesterase inhibitors (N = 38)	26 (67)		3.1 IU	

exposed jobs and are also more likely to need to change work clothes daily.

Pesticide hazards at this airport are characteristic of Central American and other developing countries where regulations or their enforcement are not adequately developed to protect workers from poisoning. Even for these highly trained workers at a work place of strategic importance for one of the country's principal sources of foreign exchange (cotton), there were no bathing facilities and the companies did not provide protective equipment. To have removed all mechanics with low cholinesterase levels from exposure would have severely compromised production at a time when it was critical to spray to control the boll weevil. Only workers with the lowest cholinesterase levels were automatically removed from production. Where possible, workers with less depressed levels were assigned to less exposed tasks, hardly an ideal solution, as all mechanic jobs involve potential pesticide exposure.

In addition, the pesticide multinationals have introduced products which are prohibited or severely restricted in the developed world, or which are not registered in developed countries and for which there is little health information available to national regulatory authorities. Although lowered cholinesterase levels reflect overexposure to, and poisonings result from, cholinesterase inhibitors, overexposure to cholinesterase inhibitors can be considered a marker for overexposure to other pesticides with chronic toxicity. Ethyl and methyl parathion are almost always mixed with the animal carcinogen toxaphene[15] in Nicaragua and were often applied with chlordimeform. Until recently, methyl parathion was involved in almost half of all poisonings reported in certain regions of the country.[11] The common practice of promoting the use of personal protective equipment (gloves and respirators) in a country where there is little personal protective equipment available, and where temperatures commonly reach 38 degrees centrigrade, is an inadequate solution to the problem of pesticide overexposure.

Nevertheless, Nicaragua appears to be taking the problem of pesticide health hazards seriously. In the past five years the government, with support from various non-governmental organizations, has initiated programs to install closed systems (which mix and load the crop dusters without the workers having to directly handle the pesticide), and has initiated training programs to protect these workers. The Ministry of Health has prohibited the mixing and loading of pesticides at this airport; the airport is to serve as a base for storage, maintenance, and repair of previously washed planes. All mixing and loading is to be done at outlying satellite airstrips, where the closed mixing and loading systems have been installed. Although in practice this may be difficult to enforce, the Ministry's order (based on concern about contamination of ground water as well as worker health) is proving to be a useful tactic in forcing the companies to cooperate with remedial action. Coveralls have been distributed to all mechanics, and free laundry service is available to most of the mechanics working at the airport. Prior to the spray season in 1988, all mechanics were released from work for a two-day training program on safe handling of pesticides. A worker health and safety committee has been established and is being trained further in basic preventive measures and in emergency treatment of poisoning from cholinesterase inhibitors. Children under 16 years old are no longer employed at the airport, and funding has been obtained for a pilot program to evaluate a new, thin (but pesticide impermeable) glove to see if it can be used for the fine manipulation of parts by the mechanics. Perhaps the most important change which may result in decreased pesticide poisoning by these workers is the decreasing amount of land planted in cotton in Nicaragua. The result may be less demand for aerial spraying and less pressure to get the maximum production from each crop duster, making it possible to enforce the washing of each plane before any maintenance is done. Finally, despite strong objections by the cotton producing industry, the importation of chlordimeform was recently halted, and a new regulation gives a commission headed by the Ministry of Health the right to veto the importation of pesticides deemed to be dangerous to public health.

APPENDIX

Pesticides Used at Crop Dusting Airport, Chinandega, Nicaragua, December 1987

Pesticides with Long-term Health Effects

Chlordimeform** (metabolite is human bladder carcinogen)[6]
Methamidophos** (human delayed peripheral neurotoxin[14])
Toxaphene** (animal carcinogen[15])
Maneb/mancozeb** (animal carcinogen[9])

Other Pesticides Restricted or Prohibited in Other Countries[16]

Methomyl**
Mephosfolan**
Methyl** and diethyl* parathion

Other Pesticides not Registered in the US

Dominex**
Bendocet**
Jupiter**

Other Pesticides of Lesser Toxicity

Acephate**
Propargite**
Chlorpyrifos**
Talstar*
Deltamethrin**
Propiconazole*
Bacillus Thuringiensis**
Lambda Cyhalothrin**

*Sprayed at one or more companies during the 30 days prior to the study but not sprayed daily by any company.

**Sprayed daily by one or more companies during the 30 days prior to the study.

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Health and Environmental Outcomes of Traditional and Modified Practices for Abatement of Residential Lead-Based Paint

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Abstract: We evaluated traditional and modified practices for abating lead-based paint in homes of children with blood-lead concentrations (PbB) > 1.4 μmol/L (> 29 μg/dl). Traditional abatement resulted in acute increases in: 1) lead contaminated house dust (generally 3 to 6-fold over pre-abatement levels, but at abated sites typically 10 to 100-fold); and 2) the PbBs of nearly half of the occupant children. Modified practices represented modest short-term improvement compared to traditional practices but were also inadequate. By six months, it was clear that neither form of abatement resulted in long-term reductions of PbB or house dust lead levels, leaving children at continued risk of excessive exposure to lead and permanent adverse neurobehavioral effects. Windows were found to be high sources of lead contaminated house dust. Recommendations are made for improved abatement practices including more complete abatement of window units and more effective clean-up to remove lead-bearing dust. Thirteen million US children live in lead-painted dwellings. Research is needed to identify abatement strategies that will be practical and well suited to the current understanding of low-level lead toxicity. (*Am J Public Health* 1990; 80:1240–1245.)

Introduction

Abatement of residential lead-based paint hazards was required more than 40 years ago in response to cases of symptomatic lead poisoning in children (generally, blood lead concentrations (PbB) > 3.86 μmol/L).* These cases were often associated with the ingestion of chips of lead-containing paint in dilapidated dwellings.[1] Together with chelation therapy, abatement of lead-based paint hazards by traditional practices in homes of children with symptomatic lead poisoning contributed to the drastic reduction in the numbers of reported lead-related deaths and recurrences of acute encephalopathy in Baltimore by the late 1960s.[2,3]

More recently, clinical and epidemiological studies have revealed that body burdens of lead previously considered safe are associated with significant long-term adverse health effects which can occur even in the absence of clinical symptoms.[4–7] Since the 1960s, the PbB considered unacceptable has been progressively lowered from 2.90 μmol/L to the current level of 1.21 μmol/L (25 μg/dl).[8–11] New concerns are being raised about the risk of adverse neurodevelopmental effects as PbBs increase above the 0.48–0.72 μmol/L range.[12–15] Lead-contaminated house dust (PbD) ingested via repetitive hand-to-mouth activity is now recognized as a major contributor to the total body lead burden of children.[16–18]

Studies in the 1980s suggest that traditional abatement practices are inadequate for reducing exposure so that children's PbBs can be maintained within acceptable levels. Chisolm, *et al*,[19] found a recurrence rate of 47 percent of PbBs greater than 2.36 μmol/L in children following chelation therapy and reoccupancy of older dwellings abated by traditional methods. Charney, *et al*,[20] showed that repeated dust removal following lead-paint abatement was associated with a modest reduction in children's PbB whereas lead-paint abatement alone was not. Various case reports indicate that abatement and refinishing activity in homes with lead-based paint can result in increased PbBs in workers and children.[21–25]

Despite changes in our understanding of the epidemiology of childhood lead toxicity and recognition of low-level adverse health effects, practices for abating residential lead-based paint have remained essentially unchanged for the last 40 years. Only recently have a small number of states established upgraded abatement requirements (Maryland, Massachusetts, Minnesota).[26–28] This paper reports on an observational prospective study in which traditional abatement practices were evaluated and compared with modified practices intended to address some of the deficiencies of traditional practices. The study was a natural experiment in which the investigators had no control over the implementation of either form of abatement.

Methods

Study Design

Serial measurements of lead in interior surface dust (PbD, mg/m^2) and children's blood were made pre-abatement, post-abatement, and six months post-abatement. A subset of dwellings abated by traditional methods had additional PbD measurements at one and three months post-abatement. Households were identified through the Baltimore City Health Department, which inspected the dwellings of children identified with lead toxicity and enforced abatement requirements. During the enrollment period (March 1984 to January 1985), property owners either performed required lead-paint abatement themselves using traditional practices or elected to have city crews perform the abatement using modified traditional practices. City abatements were being offered for the first time and were done according to principles similar to those subsequently outlined by the Centers for Disease Control (CDC).[11]

Appendix A describes and compares the two abatement practices. Unlike traditional practices, modified practices included more than minimal efforts to clean the dwelling following abatement, dispose of debris off-site, and to protect workers, occupants and their belongings. Unlike traditional practices, modified practices excluded the use of open-flame burning and sanding techniques and included the repainting of abated surfaces.

Local abatement requirements consisted of addressing deteriorated paint on surfaces up to four feet from the floor

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*To convert to μg/dl multiply by 20.72

and all paint on easily accessible "biting" surfaces where the lead content of the paint was > 0.7 mg/cm^2 by x-ray fluorescence or 0.5 percent by weight by wet chemical analysis. At the time of enrollment, toxicity was defined by the CDC as a PbB > 1.40 μmol/L (> 29 μg/dl) of whole blood together with a free erythrocyte protoporphyrin > 49 μg/dl of whole blood.[10] This study was approved by the Committee on Human Volunteers at the Johns Hopkins School of Hygiene and Public Health.

Study Sample

Seventy-one (71) study dwellings (53 traditional abatement, 18 modified abatement) had PbD measurements from pre-abatement and at least one point in time post-abatement. Attrition during the six months post-abatement was the same in both groups (17 percent).

Most study dwellings were pre-1940 row homes occupied by low-income tenants. Prior to abatement, all dwellings had multiple interior surfaces coated with lead-based paint and at least one child with PbB > 1.40 μmol/L. Based on walk-through inspections of 66 of the 71 study dwellings at the end of the study, dwellings were rated as follows using a classification system designed by housing professionals for use in this study: fairly well maintained (traditional = 8, modified = 6); substandard (poorly maintained yet maintainable: traditional = 30, modified = 10); and grossly substandard (not maintained and in need of renovation: traditional = 12 modified = 0).

Children in the 71 study dwellings abated by traditional or modified practices from which dust data were obtained, and children in an additional 25 dwellings abated by modified methods for which there were no dust-lead measurements, were included in the analysis of PbB change if they met the following criteria: age: 9 to 72 months; not known to be mentally retarded; spent 75 percent of his/her time living in the abated dwelling; resided in the abated dwelling pre- and post-abatement and had PbB determinations on venous blood at pre-abatement and at least one time post-abatement. Due to the confounding influence of chelation therapy on PbB and body burden of lead, children with histories of therapy at the time of enrollment were excluded from PbB analyses (except for the analysis of the association between PbB and PbD). PbB data were obtained by medical record review of children in the 25 dwellings abated by modified practices for which there were no dust-lead measurements.

Data Collection and Laboratory Methods

Over 3,100 dust samples were collected for lead analysis from nearly 900 sites in 71 study dwellings. From 12 to 24 dust samples were collected from the same floor, window sill, and window well (portion of window that receives the sash when window is closed) surfaces at each home visit. Samples were collected from most rooms, with particular attention to areas where children spent most of their time as reported by parents. As in previous studies[20,29,30] sample collection and preparation was done by the method of Vostal, *et al*,[31] except that no attempt was made to avoid collecting loose chips of paint and samples were analyzed using flame atomic absorption spectrophotometry at the Kennedy Institute's Trace Metals Laboratory. PbD results were expressed as mg Pb/m^2. The methods of this study underestimate the total amount of lead per surface sampled, particularly on window wells where the largest quantities of visible particulate matter and loose chips of paint were collected and the highest PbD levels were measured (see Appendix B).

Venous blood specimens were collected in low-lead vacuum tubes by the subjects' usual health care providers. Specimens were analyzed by atomic absorption spectrophotometry[32] by the Maryland Department of Health and Mental Hygiene or by anodic stripping voltammetry[33] at the Kennedy Institute's Trace Metals Laboratory using the rapid blood lead analyzer (Environmental Sciences Associates, Inc. Model 3010A, Bedford, MA). Inter-laboratory variation was minimal (data available from authors). Both laboratories served as reference laboratories for the CDC's blood lead proficiency testing program. After considering the precision of the analytical method using anodic stripping voltammetry (1 SD = 0.08 μmol/L, and modified Delves cup (1 SD = 0.16 μmol/L)[34], a change in PbB was defined as an increase or decrease of 0.24 μmol/L (5 μg/dl) or more (i.e. a change of which exceeds 1.5 to 3 standard deviations).

Data Analysis

In the absence of a federal standard for lead in interior surface dust, a target PbD of < 1.5 mg/m^2 was set for evaluation purposes. This target was based on an earlier study which reported all but one PbD level in modern suburban homes under 1.18 mg/m^2 (mean 0.29 mg/m^2).[30] Using a different method of sample collection and analysis, similar levels were reported (0.04 to 1.23 mg/m^2, GM = .20 mg/m^2) in public housing units where children were found to have acceptable PbBs (mean = 0.48 μmol/L).[35]

PbD values were found to be log-normally distributed. Units of analysis were individual PbB values and PbD values transformed using natural logarithms. PbB distributions were not log-normalized due to the restricted range of values. Multiple regression models based on maximum likelihood estimates were fit to PbB and to PbD at various points in time. Important covariates were included in the models. Since PbD values within dwellings were correlated (first order correlation coefficient for pre-PbD data ordered by household and surface type was 0.39), a correction for correlated residuals was made by adjusting the standard errors of the beta coefficients using an in-house program and retesting the significance of the variables.

Results

Dust-Lead Findings

Pre-Abatement Dust-Lead: Pre-abatement PbD levels ranged from less than 0.27 mg/m^2 to: 272 mg/m^2 on floors, 1076 mg/m^2 on window sills, and 4059 mg/m^2 on window wells. Dwellings abated by traditional and modified practices had comparable PbD before abatement (Table 1) despite differences in housing condition. Surface type and season were significant predictors of pre-PbD levels. Knowledge of which surfaces were identified for abatement was not a predictor of pre-PbD (see Table 2).

Pre-Post Change in Dust-Lead: Increased PbD levels were measured immediately following traditional abatement (usually within 48 hours) on abated window sills and on floors in close proximity to abated surfaces (Table 1). Increases at individual sites were typically 10 to 100-fold over pre-abatement levels. Most window sills (31/39) abated by the modified practices had lower PbD levels compared to pre-PbD levels. However, most window sill and floor surfaces remained outside the target range (<1.5 mg/m^2) even after final clean-up. Window wells, which were not treated during abatement by either group, had post-PbD levels which remained high in both groups (Table 1). Immediate post-abatement PbD levels in dwellings abated by modified prac-

TABLE 1—Geometric Mean (GM) Dust Lead Levels (mg/m^2) Over Time by Type of Surface and by Abatement Group

Surface Type	Abatement Group	Pre-Abatement			Post-Abatement[a]			6 Mos Post-Abatement		
		GM	95% CI	N	GM	95% CI	N	GM	95% CI	N
Floors	Traditional	2.7	(2.4,3.1)	280	15.5	(12.9,18.5)	271	3.4	(2.9,3.9)	234
	Modified	3.1	(2.2,4.2)	62	7.0	(4.9,9.9)	50	3.4	(2.6,4.5)	57
Window Sills	Traditional	14.4	(11.8,17.4)	249	38.7	(31.1,48.0)	246	16.6	(13.2,20.9)	199
	Modified	19.4	(14.6,25.9)	95	6.5	(4.8,8.8)	64	17.6	(12.4,25.0)	66
Window Wells[b]	Traditional	166.8	(124.7,223.3)	150	154.5	(120.8,197.5)	139	134.2	(97.0,185.6)	100
	Modified	196.7	(121.8,317.7)	37	87.0	(52.6,143.9)	24	267.8	(164.7,435.4)	32

[a] Post-abatement levels include values from abated and non-abated surfaces.
[b] Window wells were not abated by either group.

TABLE 2—Multiple Regression Analyses: Pre- and Post-Abatement Interior Dust Lead (mg Pb/m^2)

Independent Variables	Pre-Abatement		Post-Abatement[a]	
	Beta	(se)[b]	Beta	(se)[b]
Intercept	0.37	(0.57)	5.59	(0.56)
ln (Pre-PbD)[c]	-		0.44	(0.05)
Abatement Group				
Traditional	ref		ref	
Modified	0.31	(0.32)	−2.09	(0.36)
Surface Type				
Floor	ref		ref	
Window sill	1.54	(0.18)	−0.17	(0.17)
Window well	4.00	(0.18)	0.64	(0.21)
Knowledge of Abatement Status				
Abated surface	ref		ref	
Proximate to abated	−0.23	(0.18)	−0.55	(0.21)
Neither of the above	−0.52	(0.25)	−1.55	(0.24)
Housing Condition				
Maintained	ref		ref	
Substandard	0.25	(0.34)	0.59	(0.28)
Grossly substandard	0.52	(0.40)	0.90	(0.34)
Don't know	−0.20	(0.44)	0.79	(0.31)
Season				
Winter	ref		ref	
Spring	1.49	(0.94)	1.24	(0.27)
Summer	0.98	(0.43)	0.02	(0.30)
Fall	0.48	(0.47)	−0.21	(0.29)
Interaction				
Modified * Proximate to abated surface			1.36	(0.38)
Modified * Not abated/ not proximate to abated surface			1.94	(0.41)
n	858		726	
R^2	.56		.71	

[a] Post-PbD for modified abatements is post final clean-up level where available.
[b] Standard errors are corrected for correlated residuals.
[c] Pre-PbD distribution was centered around its geometric mean.

tices were significantly lower than post-abatement levels in dwellings abated by traditional methods after adjusting for Pre-PbD and covariates (Table 2).

Data from a subset of 19 dwellings with traditional abatement and more frequent PbD monitoring showed downward trends in PbD on floors and window sills which were greatest during the first month. Window well PbD levels remained high. By three months, PbD levels at floors, window sills, and window wells were similar to levels observed in these homes at six months and in all study homes at six months (Table 1).

Six Month Dust-Lead: At six months, PbD levels were similar to, or greater than, their respective pre-abatement levels in both abatement groups (Table 1). Also, at six months, PbD tended to increase as housing condition worsened.

Blood-Lead Findings

Of 151 children eligible for PbB analysis, 78 (52 percent) (n = 46 traditional abatement; n = 32 modified abatement) were included in at least one component of the PbB analysis. The other 73 children did not have PbB determinations on venous blood at pre-abatement and at least one point in time post-abatement due to inadequate follow-up by their health care providers. No evidence was found for differences in PbB follow-up by abatement group, sex, age, race, season, housing condition, history of chelation, or location of child during abatement. Insufficient data precluded a comparison of pre-PbB levels by follow-up status.

Pre-Abatement Blood-Lead: Children from dwellings abated by traditional and modified practices had comparable pre-abatement PbBs (see Table 3) and comparable ages at abatement (traditional: 34.6 months, modified: 34.0 months). No differences were found in Pre-PbB by sex or by housing condition.

Post-Abatement Blood-Lead: Within one month of abatement, children in traditionally abated dwellings had significantly higher PbBs than children living in dwellings abated by modified practices (see Table 3). Individual increases in PbB were observed across a range of pre-PbB values from 1.16 to 2.51 μmol/L) (24 to 52 μg/dl). Overall, 13/27 (48 percent) of children in dwellings abated by traditional practices had PbB increases (defined as 0.24 μmol/L or more). Of these, nine were hospitalized for the first time for chelation therapy (PbB > 2.36 μmol/L). Of 19 children in dwellings abated by modified practices, three (16 percent) had PbB increases, two of whom were hospitalized for the first time for chelation therapy. Children with reported home contact during abatement had significantly higher post-PbB

TABLE 3—Pre- to Post-Abatement Change in Blood Lead Concentration for Children Never Chelated Pre-Abatement

	Blood Lead (μmol/L)				
	Pre-Abatement		Post-Abatement[a]		
	$\bar{X}$	(se)	$\bar{X}$	(se)	Difference (95% CI)
Traditional Abatement (n = 27)	1.78	(.07)	2.11	(.13)	+0.33 (0.13, 0.53)
Modified Abatement (n = 19)	1.66	(.10)	1.71	(.12)	+0.05 (−0.09, 0.19)

[a] Post-abatement = within 1 month

than children with no reported contact (mean difference +0.35 µmol/L). In regression analysis ($n = 46$ children, $R^2 = .65$), abatement group was a significant predictor of post-abatement PbB after controlling for pre-PbB, season and whether or not the child had contact with the home during abatement.

Six Month Blood-Lead: At six months, children (traditional = 14, modified = 15) with no history of chelation therapy (PbB < 2.36 µmol/L) continued to have elevated PbBs (mean = 1.48 µmol/L) which were not significantly different from their pre-abatement PbBs (mean = 1.57 µmol/L). By six months post-abatement, five other children (three traditional abatement, two modified abatement) had experienced PbB > 2.36 µmol/L and had received chelation therapy.

Correlation between PbD and PbB: At pre, post, and six months post-abatement, children's PbBs were significantly correlated with floor and window sill PbD in their homes (Table 4).

Discussion

High levels of lead in dust were measured in homes of children with PbB > 1.4 µmol/L. Before and after abatement of lead-paint, 71 study dwellings had geometric mean PbD on floors, window sills, and window wells that were approximately 10 to 600 times greater than the PbDs reported by others in modern suburban homes and in public housing units where children had acceptable PbBs.[30,35] Study homes in the most deteriorated condition tended to have the highest PbD levels over time and the highest risk of chelation therapy (PbB > 2.36 µmol/L) among occupant children. These homes had multiple problems such as roof and plumbing leaks, holes in walls, deteriorated floors, and defective heating systems.

Most components of windows were not abated of lead-paint, and window wells remained reservoirs of very high levels of PbD during the entire study period regardless of housing condition. Most windows in study homes were deteriorated and within easy reach of young children. We observed that repeated opening and closing of old windows resulted in further deterioration of lead-painted surfaces on interior and exterior window components and contributed to the accumulation of visible dust and chips of paint on window wells. Higher interior PbD levels observed during spring and summer may be related, in part, to more frequent opening and closing of windows by occupants during these seasons. Others have also reported differences in PbD levels by season, housing characteristics, and location within rooms.[29,36,37] Soil lead was not measured in this study, although others have reported significant correlations between concentrations of lead in surface soil and interior house dust.[16,37]

Despite the implementation of improved practices, modified abatements, like traditional abatements, did not result in any long-term reductions of levels of lead in house dust or the blood of children with pre-abatement PbBs between 1.16 and 2.51 µmol/L. Traditional abatement practices also resulted in acute increases in PbD and the PbBs of children. Some received chelation therapy (PbB > 2.36 µmol/L) for the first time following abatement. With alternative abatement practices children were less likely to experience acute increases in PbB. However, post-abatement PbD levels overall exceeded the target range (<1.5 mg/m^2) despite improvements in PbD levels at most abated sites. Household respondents reported that one-third of children in both abatement groups had some contact with the home during abatement (day, night, or both) against the advice of the city health department. Home contact was associated with significant increases in children's PbB in this and other reports.[24,25] As in previous studies, a significant relationship was found between PbB and dust-lead levels.[36–38]

Inskip and Atterbury have reported high rates of deposition of lead on surfaces in close proximity to surfaces abated by methods used in this study as follows: heat gun and torches: 1 to 5 mg Pb/m^2/hour, sanding: 50 to 200 mg Pb/m^2/hour.** One dwelling in this study abated by open-flame burning and sanding was noteworthy because two study children and a third who moved into the dwelling after abatement had a total of five admissions for chelation therapy (PbB > 2.36 µmol/L) during the entire post-abatement study period.

In addition to the use of high dust-generating methods, poor containment, clean-up, and disposal practices associated with traditional abatements (Appendix A) exacerbated the problem of exposure to lead-bearing dust on household surfaces. Exposure to lead-bearing dust is particularly hazardous for children because hand-to-mouth activity is recognized as a major route of entry of lead into the body and because absorption of lead is inversely related to particle size.[39] Another study[40] showed that 21 percent of lead in house dust was found in particles of size less than 44 microns. This suggests that standard vacuums used by city crews in performing modified abatements may not have been adequate to trap lead-bearing particulates which may have been

TABLE 4—Pearson Correlation (r) Over Time: Children's Blood Lead Concentrations and Geometric Mean Dust-Lead Levels in Their Homes

	Floor PbD			Window Sill PbD		
Blood Lead	r	95% CI	n	r	95% CI	n
Pre-Abatement[a]	0.35	(.08, .57)	50	0.31	(.04, .54)	50
Post-Abatement[b]	0.48	(.20, .70)	37	0.40	(.07, .66)	33
6 Months Post-Abatement[c]	0.54	(.23, .76)	30	0.53	(.18, .75)	27

[a] Includes children chelated pre-abatement (admission PbB value used) and children with no history of chelation therapy pre-abatement.

[b] Includes children chelated and discharged to abated dwellings who had re-exposure defined as PbB rebound followed by an increase in PbB to or above prior admission level with subsequent readmission (readmission PbB used for six children in floor PbD:PbB correlation and for four children in window sill PbD:PbB correlation).

[c] Includes children with no history of chelation and children six months post-chelation.

**Inskip M, Atterbury N: The legacy of lead-based paint: potential hazards to "do-it-yourself" enthusiasts and children. Proceedings of the International Conference on Heavy Metals in the Environment. Heidelberg, West Germany, 1983. CEP Consultants, Ltd., Edinburgh, UK, pp. 286–289.

exhausted, re-entrained into the air, and redeposited.

PbD levels and the ability to reduce them appear to be related to the condition of household surfaces. Within and across study dwellings, smooth floor surfaces (e.g., vinyl tile, linoleum) tended to have lower PbD levels than wooden floors, which in our study sample were usually pitted, splintered, and worn. A relationship between surface condition and effectiveness of clean-up was found in subsequent studies which covered or coated old floors prior to final clean-up.***

The lack of long-term effectiveness for reducing lead exposure may have been due to the reliance upon abatement of certain surfaces up to four feet from the floor that children could easily reach, mouth, and chew. In this respect both the traditional and modified abatement practices reflected an outdated understanding of the etiology of childhood lead poisoning. These limited forms of abatement did not address high sources of lead-contaminated dust such as windows and left the potential for ongoing exposure to lead in paint and dust. Poorly maintained housing was observed to deteriorate further after abatement. Poor containment and clean-up practices during abatement may also have contributed to increased and ongoing exposures to lead-bearing dust on upholstered furnishings and in air ducts and vents.

Lead in paint, dust, and soil now constitute the major sources and pathways of lead exposure for US children. Recent estimates are that 42 million US dwellings contain lead-based paint, and 1.8 million US children live in deteriorated homes with lead-paint.[18] The public health goal vis-a-vis lead toxicity in children is to maintain PbBs of children and fetuses below levels associated with adverse health effects (i.e. PbB below 0.48–0.72 μmol/L).

There is a need for a new approach[41] to abating residential lead-based paint which would include: 1) more extensive, if not complete, abatement of lead-paint on interior and exterior surfaces using replacement, paint removal and encapsulation methods which prove to be safe, practical and effective in the long-term; 2) the reduction of lead-bearing house dust by the application of the following: (a) more effective clean-up measures which may well require the use of vacuums equipped with high efficiency particle air (HEPA) filters, (b) proper disposal of abatement waste, (c) the use of engineering and work practice controls to minimize and contain lead-dust produced during abatement, and (d) upgraded work practices to protect workers, occupants, their belongings, and the environment; 3) post-abatement clearance testing of lead in interior surface dust prior to reoccupancy; and 4) evaluation of costs and health and environmental outcomes of alternative abatement methodologies. The findings of this study have provided the basis for studies now in progress based upon the principles just cited. This new approach also provides for temporary relocation of families and their belongings to safe housing during abatement; worker education, training and certification; and takes into account the overall condition of dwellings, the conditions of specific painted surfaces and substrates, and other needed repairs as adopted in part in recent state regulations.[26,27] Post-abatement clearance testing for interior dust-lead prior to reoccupancy has been introduced recently in Maryland and Massachusetts using interim state standards.[26,27]

The role of lead-dust and hand-to-mouth activity in childhood lead poisoning was first recognized by Gibson in 1904.[42] In applying this knowledge to a new approach to abatement, we would do well to consider the following which Benjamin Franklin wrote in a letter to Benjamin Vaughan in 1786:

> "You will see by it that the Opinion of this mischievous Effect from Lead, is at least above Sixty Years old; and you will observe with Concern how long a useful Truth may be known, and exist, before it is generally receiv'd and practic'd on."

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APPENDIX A

Comparison of Traditional and Modified Abatement Practices

	Traditional Abatement	Modified Abatement
Extent of abatement	Up to 4 feet from floor	Up to 4 feet from floor[a]
Methods	Torch and/or sander	Heat gun
Repainting	No	Yes
Clean-up	Minimal[b]	Thorough[c]
Disposal or debris	Haphazard[d]	Off-site
Worker protection	Minimal[e]	Adequate[f]
Occupant Protection	Minimal	Some[g]
Protection of belongings	Minimal	Some[h]
Supervision of workers	No	Yes[i]

[a] Interior side trim of windows was also abated above four feet from floor.

[b] Typically dry sweeping, if done at all.

[c] Wet cleaning with high-phosphate detergent together with dry vacuuming using standard shop vacuums.

[d] Abatement debris was often left uncontained inside or outside of the home.

[e] No or inadequate respiratory protection; no blood-lead monitoring; often no protective clothing and gear.

[f] Workers were trained in use of respirators, fit tested, and provided with half mask air purifying respirators with high efficiency particle air (HEPA) filters. Overalls were provided and laundered regularly; blood lead monitoring was done.

[g] City crews had better clean up practices, and were more likely to warn parents of hazards and provide instructions on dust control. However, children in both abatement groups had some contact with the home during abatement.

[h] Furnishings and some floors were covered with tarps and kitchen items and clothes were stored in sealed closets and cabinets.

[i] City crews were supervised on-site during abatement.

APPENDIX B

Efficiency of Collection and Analysis of Lead in House Dust

Sampling was done on abated and non-abated surfaces by wiping with alcohol impregnated towelettes (14.6 cm × 20.3 cm). Dust was collected from 0.09 m^2 (one square foot) of floor surfaces using a template. Window sills and window wells were measured and alternate halves were sampled at each visit. Surfaces were wiped back and forth twice in each direction and the procedure was repeated after folding the towelette in half.

Sampling efficiency was assessed by rewiping the same surfaces up to 10 times. Sampling efficiency of a single towelette appeared to be positively related to the degree of smoothness of the surface and inversely related to the loading (total mass) on a surface. When the PbD level was less than 1.0 mg/m^2 on an initial wipe from smooth surfaces with no visible chips of paint, then non-detectable levels (<0.5 ppm lead in 20 ml extractant), or levels just above them, were usually found on the second or third towelette. When the PbD level was greater than 100 mg/m^2 on an initial wipe, and when chips and/or particulates were visible, then PbD levels greater than 10 mg/m^2 were usually detected through at least the tenth towelette.

Efficiency of elution was inversely related to the ratio of mass of sample to mass of extractant (s/e ratio). Elution efficiency at the Trace Metals Laboratory was as follows for the following standard reference materials (SRM) of the National Bureau of Standards: Urban particulate SRM #1648 (0.655 percent lead by weight): 69 to 100 percent as s/e ratio ranged from 1:67 to 1:6667; Paint SRM #1570 (11.87 percent lead by weight): 24 to 93 percent as s/e ratio ranged from 1:76 to 1:2083; Orchard leaves (use due to high silica content) SRM #1571 (45 μg Pb/g): 32 to 58 percent as s/e ratio ranged from 1:14 to 1:21.

Placing Patients in the Queue for Coronary Revascularization: Evidence for Practice Variations from an Expert Panel Process

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Abstract: A panel of 16 cardiologists and cardiac surgeons rated 438 case scenarios for the maximum acceptable delay prior to revascularization, using a scale with seven interventional time frames and two nodes for designating dubious or inappropriate cases. If consensus was defined as agreement by 12 or more panelists, only 1.4 percent of the case scenarios showed consensus on a single rating. Dividing the scale into three broad clinical categories (revascularize promptly, place on a waiting list, or no intervention), 11.4 percent of scenarios showed all 16 panelists agreeing on a single category, rising to 59.4 percent of scenarios if agreement by 12 panelists was accepted as a consensus. The mean difference between the panelists' highest and lowest urgency ratings yielded waiting time differences of two weeks for scenarios of very unstable angina, and more than three months for those with stable angina. However, in a regression model, individual panelist factors on average had less effect than clinical features such as severity and stability of angina, or stenosis of major coronary arteries. These findings strongly support the need for consensus criteria to ensure that triage practices are consistent and fair, and also suggest that widespread adoption of a standardized approach to revascularization priorities may be feasible (*Am J Public Health* 1990; 80:1246–1252.)

Introduction

In many countries, limits on medical facilities and manpower make it difficult to offer rapid coronary revascularization procedures to all patients with coronary heart disease who might benefit. Cardiac surgeons and cardiologists currently assess patients according to various informal criteria in an attempt to ensure that persons with more symptoms or a higher time-dependent risk of ischemic events are revascularized expeditiously—a sorting process generally termed triage. However, no formal schema for revascularization triage has been accepted or even proposed in such a fashion as to generate widespread debate.

In the Canadian province of Ontario, waiting lists for elective coronary artery bypass surgery [CABS] during 1988 ranged between two and twelve months in five of nine hospitals with open heart surgery facilities, and the three cardiac surgery centers in Toronto had a combined waiting list of 848 patients as of January 1989.[1] These waiting times have created an ethical imperative to ensure that patients with symptomatic coronary disease at least receive attention according to perceived urgency of clinical need. Providers and the provincial government therefore agreed that formal triage criteria should be developed and applied in a pilot project for Toronto-area hospitals. To arrive at a consensus about guiding clinical principles in this area of practice, an expert panel of cardiologists and cardiac surgeons was convened. We postulated that the lack of accepted criteria for triage might be associated with considerable interpractitioner variation in whether—and where—patients were placed in the waiting lists for coronary revascularization. The formal group process followed by the panelists generated evidence about the nature and extent of inter-practitioner agreement and disagreement. We herein present this evidence and discuss its implications for promotion of a uniform approach to triage practices.

Methods

Panel Process

The group process followed by the revascularization panel was a variant on techniques used by researchers at the RAND Corporation[2–4] and the Canadian National Consensus Conference on Aspects of Cesarean Birth.[5,6] The 16-man panel included five cardiovascular surgeons from academic centers; six cardiologists practicing in academic centers, three of whom had extensive experience with percutaneous transluminal coronary angioplasty [PTCA]; and five cardiologists practicing in community hospitals that refer patients to the Toronto academic centers offering CABS or PTCA (Appendix A). Drawing on pre-circulated background materials, the panelists met for a day in October 1988 and agreed on factors that would be most important in determining urgency of need for revascularization; levels within each factor were also set out (Appendix B). An urgency rating scale was adopted, with several time-frames for revascularization and two appropriateness ratings for indicating those instances where triage to revascularization seemed questionable or contraindicated (Appendix C).

After the first panel meeting, an Urgency Rating Questionnaire was compiled, permuting the factors agreed upon by the panelists into patient case scenarios. Implausible scenarios were eliminated, and levels of given factors deemed unlikely to affect decision-making were eliminated or combined, leaving 438 separate case scenarios (sample materials available on request). Case scenarios were oriented primarily to urgency ratings, in that all patients had at least significant single vessel disease and all were presumed to have clinically unequivocal angina. The questionnaire was organized into five chapters according to the level of what was *a priori* believed to be the most important factor—the pain syndrome, defined as the severity or stability of anginal symptoms, and

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response of those symptoms to medical therapy (Appendix B).

The panel had agreed that a single set of criteria would be developed for revascularization in general, pending the later generation of a separate set of triage criteria for PTCA. Panelists were therefore to rank scenarios with a view to employing either PTCA or CABS, depending on the clinical features. The majority of scenarios, however, were anatomically appropriate for CABS rather than PTCA (Appendix B). Panelists were instructed that the waiting period should be that deemed reasonable given: the presumed risk of death from ischemic events due to delayed revascularization, as suggested by clinical experience and evidence from a precirculated literature review; the presumed ongoing morbidity as a result of anginal symptoms; and other relevant factors as determined by the individual panelist. They were specifically enjoined to approach the questionnaire with an understanding that resources for coronary revascularization were in competition with other worthy programs. The waiting period was presumed to start from the time that anatomical data from angiography were available in the presence of appropriate symptoms of angina.

To help ensure a shared body of knowledge, a literature review was compiled to accompany the Urgency Rating Questionnaire. This review focused on any known temporal differences in risk of death from ischemic events for patients receiving medical rather than surgical therapy, and was organized according to each of the agreed-upon factors, singly and/or in combination with other factors. Panelists were urged to read the document prior to completing the questionnaire, and were also supplied with an executive summary of it for ease of reference.

Our process differed from that developed by the RAND researchers in two key respects. The Ontario triage panelists met initially to agree on the scale and the factors to be incorporated into the Urgency Rating Questionnaire, completed the questionnaire, received by mail their individual ratings as compared to all other panelists, and finally met again to arrive at consensus criteria for triage practices. This process actually reduced one potential source of inter-practitioner disagreement—rejection of the plausibility of either the factors used to construct the case scenarios, or the combinations of factors into particular case scenarios. In contrast, Park, *et al*, report that indications lists were substantially revised by the RAND panelists when they met to review their appropriateness ratings for various case scenarios.[2] The other difference in process was re-rating of scenarios. The RAND panelists rated their scenarios twice: first independently, and again at a panel meeting, taking into account their results as compared to other panelists. The Ontario panelists rated scenarios once, without knowledge of their peers' ratings.

Statistical Analysis

With 16 panelists rating 438 case scenarios, there were only eight missing ratings out of a possible 7,008; appropriate allowance was made for them in all analysis. Descriptive measures of agreement and disagreement are explained with the relevant results. More formal statistical analysis involved two methods: an index of agreement for multiple raters and intraclass correlation coefficients.

The agreement index (Appendix D) was constructed to estimate the probability that two randomly chosen panelists, drawn without replacement, would agree on the classification of a randomly chosen scenario. This index—termed P_a—was calculated for the entire set of scenarios, and for each level of angina symptomatology, hereafter termed, "pain syndrome." Agreement was calculated both for exact scale ratings and within three sets of scale ratings (raings 1–4, 5–7, and 8–9) representing similar clinical decisions. The agreement ratings are reported both as overall levels of agreement and corrected for chance agreement between panelists, i.e., a kappa correction.[7] This correction reduces the agreement probability by accounting for the overall likelihood of any two raters agreeing by chance, given the overall pattern of responses across the entire set of 438 scenarios.

The indices of agreement do not penalize panelists for greater scale disagreement. That is, be it with respect to exact agreement or agreement by approximate clinical approach, two randomly drawn raters scoring a scenario for intervention within 24 hours ("extremely urgent") versus intervention within 3–6 months ("marked delay") are both recorded simply as disagreeing, but the extent of this discrepancy is not captured. To reflect the ordinal nature of the rating scale, intraclass correlation coefficients [ICCs] were calculated.[8] Analogous to weighted kappa statistics, the ICCs show the expected numerical correlation between the ratings of two randomly chosen panelists rating the same randomly chosen scenario. For ease of analysis, we assume that the two non-interventional ratings ("questionable" and "inappropriate") follow after the final time-node, "marked delay." This simplifying assumption tends to increase the correlation between panelists' ratings in case scenarios with scores reflecting low urgency, and reduces correlation in scenarios with high urgency. However, differences between "inappropriate" and "marked delay" are arguably much less important than between the former and "extremely urgent."

Linear regression analysis[9] was also performed to estimate the relative impact of practitioner versus clinical factors. To facilitate analysis, the entire scale was again treated as ordered (see above for justification).

Results

Descriptive Grouping of Ratings

For each scenario, one may either consider the number or proportion of panelists agreeing on a given set of contiguous rating categories (scale agreement) or the number of contiguous ratings required to encompass the ratings of a given number of panelists (panel agreement). Thus, consensus consists of panel or scale agreement, or both. Complete agreement on a single rating by all panelists never occurred. If the definition of panel agreement was relaxed to include as few as 12/16 panelists, i.e., agreement by at least 75 percent of the panel, then only 6/438 (1.4 percent) of the case scenarios showed consensus on a single rating. With a further relaxation of the definition of panel agreement, to a simple majority or ≥ nine panelists, agreement on a single rating rose to 102/438 scenarios (23.2 percent). Relaxed definitions of scale agreement were also applied, with the entire nine-point scale taken as contiguous. To encompass the responses of all panelists 50 percent of the time, it was necessary to relax the definition of scale agreement to five contiguous points. On the other hand, by allowing some latitude in definitions of both scale and panel agreement, frequent clustering of responses was evident. For example, at least three-fourths of panelists agreed within a three-point range in over 80 percent of cases.

Indices of Exact Scale Agreement

The probabilities that any two randomly drawn panelists would agree on a particular rating for a given scenario are shown in Table 1 according to each pain syndrome and overall. The exact agreement is consistently at the 25–30 percent level, falling somewhat only for the highest urgency scenarios—unstable angina with persisting symptomatology requiring parenteral therapy for control. The degree of agreement corrected for chance is poor.

Because our primary concern was with urgency rather than appropriateness, these indices were recalculated including only the time-related ratings between "emergency" (node 1) and "marked delay" (node 7), i.e., eliminating appropriateness as a source of disagreement. The resulting agreement on urgency ratings ran 30–40 percent, and was only moderately higher than in the total scale case (data available on request to author).

Indices of Approximate Scale Agreement

Clinical divisions: The first four ratings on the scale (Appendix A) imply that patients will be revascularized on the same admission if hospitalized for medical therapy or catheterization, or readmitted within two weeks; whereas the next three ratings will be on outpatient waiting lists. We term these two categories respectively "DO" and "WAIT", and the last two non-interventional ratings, "NOT".

Only 11.4 percent of scenarios showed all 16 panelists agreeing within one of these three clinically pertinent categories. However, if panel agreement was re-defined as congruence among ≥12 clinicians, categorical agreement was found for 59.4 percent of scenarios. Moreover, as shown in Table 1, the overall P_a increased greatly, rising to about 65 percent. Thus, there was evidence of a general agreement on a general approach to these patients. The probabilities of agreement between two randomly drawn panelists were even higher (82 percent) when appropriateness ratings were eliminated, leaving only the clinical dichotomy of "DO" versus "WAIT" (data on request to author).

When divided by pain syndrome, the indices reveal a significantly higher degree of agreement for the most unstable patients—the opposite of the trend when exact agreement was sought (Table 1). This enhanced agreement for an overall approach was attributable to the fact that patients still on parenteral therapy obviously could not be discharged from hospital, would almost invariably fall into the "DO" category, and only occasionally be rated as "WAIT". The lower index for the exact ratings was due to poor agreement among panelists within the first four ratings; only four panelists rated any scenarios at node 1 ("emergency").

It should be noted that there was considerable difference among panelists in frequency of use of "NOT" ratings—"questionable" or "inappropriate". While 10 panelists rated between 49 and 105 scenarios in "NOT" categories, the extent of disagreement about appropriateness is suggested by the fact that the other six applied "NOT" ratings to 1, 20, 37, 135, 172, and 200 scenarios respectively. One way of examining divisions of opinion about appropriateness is to consider the proportions of scenarios where ≥4 panelists rate "DO" and ≥4 rate "NOT". Broken down by pain syndrome, the percentages of scenarios with this pattern of disagreement were as follows: mild to moderate stable angina, 4.5 percent; severe stable angina, 1.6 percent; unstable angina with adequate restabilization on oral medical therapy, 4.4 percent; unstable angina with incomplete stabilization on oral medical therapy, 24.2 percent; and unstable angina requiring ongoing parenteral medication, 16.7 percent. Note that the latter two sections of the Urgency Rating Questionnaire were actually identical apart from the pain syndrome. The reduced frequency of "NOT" versus "DO" disagreement was accordingly due entirely to the fact that patients requiring parenteral therapy were believed so ill that the risk-benefit ratio of revascularization was deemed more uniformly acceptable, leading to greater consistency in application of "DO" ratings.

Numerical Scale Association: Intraclass correlation coefficients are also displayed in Table 1. When separated by the five levels of pain syndrome, the intraclass correlations sharply decrease with more severe or unstable angina. This is similar to the situation for exact scale agreement using the non-ordinal index of agreement, and is due to clustering of ratings (e.g. 88 percent of panelists' ratings are between time-nodes 1 and 4 for the most severe pain syndrome). Hence, while there is relatively low variability between scenarios, there is also little overall agreement on the exact timing of revascularization. As well, any disagreement about appropriateness further reduces the correlation coefficient, because of numerical distances between scale points under an assumption of ordinality (e.g., time-nodes 1-4 versus non-intervention nodes 8-9).

Agreement and Disagreement by Individuals and Subgroups

There were no significant differences in total absolute distance from the median scenario ratings or frequency of

TABLE 1—Agreement on Urgency/Appropriateness Rating

	Stable Angina Symptoms on Medical Therapy		Unstable Angina Symptoms on Medical Therapy			
	Mild-moderate	Severe	Resolved	Partly Resolved	Persisting	Overall
Exact						
P_a[*]	0.30	0.31	0.29	0.30	0.25	0.29
SE (P_a)	0.01	0.01	0.01	0.01	0.01	0.01
Kappa	0.18	0.19	0.17	0.18	0.12	0.16
Clinical Category[#]						
P_a	0.58	0.65	0.56	0.56	0.81	0.65
SE (P_a)	0.02	0.02	0.02	0.01	0.01	0.01
Kappa	0.33	0.44	0.30	0.29	0.70	0.43
Scale Correlation ICC[+] (random effects)	0.49	0.51	0.40	0.16	0.13	0.51

[*] P_a = probability of agreement for two randomly drawn raters on a randomly chosen scenario; the kappa correction is unweighted. [#] Scale collapsed into three clinical categories, "DO" within two weeks (time-nodes 1–4); "WAIT" up to six months (time-nodes 5–7); and "NOT" triaged (ratings 8 for "questionable" or 9 for "inappropriate"). [+] ICC = intraclass correlation coefficient, analogous to a weighted kappa.

outlier status (defined as being greater than one scale point from the median rating) according to practitioner experience, academic or non-academic center for practice, and surgical versus cardiological orientation.

The Practitioner Factor in Context

We used regression techniques to determine, within each pain syndrome and for each practitioner, the influence of practitioner variability as opposed to that stemming from the clinical factors incorporated into the questionnaire. Results for the three panelists with largest and smallest absolute coefficients are shown in Table 2, showing respectively systematic departure from, and congruence with, the mean ratings of the group for any given scenario.

Table 3 presents the regression coefficients for various clinical factors, as well as the median absolute value of the panelist coefficient for each pain syndrome. As suggested by the change *across* chapters due to the pain syndrome alone, this was the dominant determinant of ratings. The influence of the panelists is suggested by comparing the magnitude of the regression coefficients for clinical factors *within* any given pain syndrome to the regression coefficients for the median panelist. The latter is significantly smaller than key clinical variables such as pain syndrome or stenosis of major coronary arteries (standard errors are approximately 0.10 for all coefficients, including the panelist factor.) However, as indicated in Table 2, some panelists did systematically differ from the mean panel rating to a much greater extent.

Urgency Rating Discrepancies in Isolation

Beyond the indices of agreement on urgency ratings calculated above, we sought also to quantify the extent of discrepancies among panelists rating a given scenario between 1 and 7. Two measures were calculated: the maximum discrepancy of ratings within each scenario, and the discrepancy between the extreme ratings when the highest and lowest 25 percent of ratings were eliminated for each scenario. (The number of ratings deleted at each extreme of the sorted ratings was the largest integer less than or equal to the total number of ratings/4). All urgency ratings could, on average, be contained within 3.5 points on the scale, while the majority could be contained in less than two points on average. These results are displayed in Table 4.

TABLE 2—Influence of Panelists on Ratings: Regression Coefficients for Panelists with Least and Greatest Systematic Departure from Group Mean

	Level of pain syndrome*				
	1	2	3	4	5
Greatest Influence					
	−1.14	−0.84	−1.14	1.32	1.79
	0.66	0.82	1.31	1.79	0.84
	−0.93	−0.87	−0.47	−1.71	−1.42
Smallest Influence					
	−0.32	0.35	0.30	−0.31	−0.20
	0.07	0.27	0.14	0.24	0.11
	0.19	−0.04	−0.11	−0.31	−0.14
Standard Errors	0.12	0.11	0.13	0.11	0.14

*Levels of pain syndrome are in the same order as Appendix B. Note that a positive coefficient implies higher numerical score, i.e., less aggressive management; a negative coefficient has the opposite implication. Coefficients reflect influence within a model where, theoretically, the minimum value possible is 1.0 and the maximum is 9.0. However, no mean scenario rating was ever <2.0 and only a few within the mildest pain syndrome exceeded 8.5.

TABLE 3—Impact of Various Factors on Mean Ratings: Regression Coefficients

Chapter of questionnaire	1	2	3	4	5
Pain Syndrome (base case for other factors)*	8.01	7.09	6.98	4.19	2.83
Univariate Departures from Base Case					
Anatomy					
Left main disease	−2.57	−2.34	−2.06	−1.33	−1.05
3 vessel disease	−1.09	−0.53	−1.06	−0.57	−0.54
Left Ventricular Function					
Grade IV	0.08	0.10	0.28	0.77	0.73
Non-invasive Tests					
High risk	−1.34	−1.07	−1.20	NA	NA
Recent MI	NA	NA	NA	0.16	0.26
Previous CABS	NA	NA	NA	0.44	0.49
Median Panelist (absolute value)	0.55	0.33	0.49	0.40	0.31

Notes: Definitions for clinical factors are explained in Appendix B. The model presupposes a baseline case incorporating the pain syndrome. For pain syndromes corresponding to angina classes I-II, III, and IVA, the baseline anatomic factor is single or double vessel disease without left anterior descending arterial stenosis; left ventricular function is graded I-II; non-invasive tests suggest a low or average ischemic risk; and the expected procedural morbidity and mortality is low. For unstable angina without adequate symptomatic stabilization (classes IVB and IVC) neither non-invasive tests nor the distinction between left ventricular grades I and II apply, and the relevant base case is "No recent myocardial infarction" and "No previous CABS." All standard errors are approximately 0.10 (ranging between 0.05 and 0.14) except for Left ventricular grades I and II, where the standard error within angina class IVA is 0.19 in both cases. The coefficients for univariate changes in baseline factors illustrate their influence within a given pain syndrome.

TABLE 4—Widths of Ranges Encompassing Urgency Ratings in Isolation

Minimum number raters rating 1–7 for inclusion of the scenario	No Minimum	≥8 Raters	≥12 Raters
Number scenarios	438	392	327
Mean number rating "1"–"7"	12.85	13.84	14.65
Range (all raters)	3.55	3.69	3.72
Range (trimmed of high and low quartiles)	1.92	1.93	1.90
Mean residual number of ratings in trimmed result	7.12	7.59	7.95

Discussion

Although American[10] and British[11] RAND panels have previously graded the appropriateness of CABS, those evaluations were based upon 1981 indications, and involved ratings on a nine-point appropriateness scale—clearly distinct from our urgency scale with seven different time intervals and two appropriateness categories. It is nonetheless illuminating to compare similar agreement indices for our 16-person panel to those reported for the nine-person RAND panel. If unanimity is sought, the inter-practitioner agreement of the triage panel is about on a par with the first ratings of the RAND panel, and significantly lower than occurs with a second rating by the RAND panel once they knew their colleagues' ratings. However, in a comparison excluding extreme high and low ratings, agreement among the Ontario triage panel is superior to the first ratings and about on a par with the second ratings of the RAND panel (data available on request). This suggests an influence of outliers in the Toronto panel.

We have two suggested explanations for the outlier phenomenon. The first is that the structure of the scale may have been contributory. That is, outliers will be created when some panelists rate a scenario as relatively urgent (time-nodes 1 to 4) while others question the risk-benefit ratio and need for intervention (ratings 8 and 9). The second possibility is that a larger panel may increase the likelihood that one or more panelists will produce idiosyncratic ratings for any given scenario. We could not detect effects according to practitioner experience, site of practice (academic versus non-academic), or surgical versus cardiological orientation. However, the actual number of raters in any identifiable subgroup was small enough to limit our statistical power for detecting such effects.

Because our ratings reflect the initial clinical judgments of cardiologists and cardiac surgeons in the absence of knowledge about their peers' ratings, they offer an indication of the extent of inter-practitioner variation that might occur in actual practice. Moreover, inter-practitioner variation in ratings would be minimized by several features of the exercise followed here. All panelists practiced in urban centers, and were Canadian-certified specialists in cardiology or cardiac surgery. The majority did some specialty training at the University of Toronto, and practiced in or near Metropolitan Toronto. All received the same literature review summarizing how various factors influenced any time-dependent risk of death or myocardial infarction stemming from delay of mechanical revascularization. As already noted, all had agreed to the factors that were to be considered in rating case scenarios, and rated patients according to a standardized scale. All reviewed exactly the same case material, with none of the discrepancies that might occur in actual practice when different doctors assess patients and their test results. It is therefore very unlikely that the results of this exercise over-estimate the extent of inter-practitioner variation in managing this patient population. We suspect that larger discrepancies would be demonstrable on review of actual triage practices in Canada and other countries.

The magnitude of those discrepancies, as demonstrated here, is striking. Consider the following three examples from our results. First, even if agreement among a simple majority of panelists was accepted as reasonable, convergence on a single rating occurred in only 23 percent of scenarios. Second, if we divided the scale into three broad clinical categories—i.e. revascularize promptly, place on a waiting list, or do not plan intervention—only 11.4 percent of scenarios showed all 16 panelists agreeing within one of the three clinically pertinent categories. Third, even after eliminating disagreement about appropriateness of revascularization, the average difference between highest and lowest urgency ratings for the scenarios was 3.5 scale points out of a possible 7—corresponding to time differences ranging from two weeks for the most unstable patients, and on out to more than three months for those with stable angina.

In our view, these discrepancies are at odds with the aims of Canada's universal health care system. The architects of the Canadian health insurance system emphasized the concept of fairness, with the goal being that citizens should receive health services according to their needs.[12] A potential drawback to national health care systems is centrally constrained resources, with the substitution of rationing by queue for the rationing by price or income that occurs in settings of private prepayment for medical services; this criticism has been leveled against the British National Health Service.[13] However, one off-setting advantage of rationing by queue is that physicians are able to rank order patients in the queue according to judgments about the urgency of clinical need—arguably a fairer approach than priorities based on incomes or influence. Our findings raise the concern that this potential advantage is not being fully realized for coronary revascularization in the Canadian system.

While appropriateness issues were not the focus of this exercise, one logical line of attack on waiting lists is to ensure that all those waiting would indeed benefit from planned procedures. The CABS rates in Ontario have plateaued over the last several years. Anderson and Lomas have observed that the rates are being maintained largely by increasing application of CABS to patients over 65 years of age.[14] It is unclear whether the increasing use of CABS in the elderly represents an extension of utilization patterns to a group with a less favorable risk-benefit ratio, or an appropriate shift in utilization as the procedure becomes safer for elderly patients. The inter-rater disagreement on appropriateness ratings observed here suggests that a formal appropriateness panel may also prove worthwhile. In any event, creation of a fairer and more rational queue is a logical complement to any strategy that seeks to optimize resource utilization.

Despite the above-noted variations, at least three-fourths of panelists did agree within a three-point range on the urgency rating scale in over 80 percent of cases. When clinically pertinent categories were considered, any two randomly drawn panelists would rate scenarios in the same category two out of three times. Furthermore, weighed against the clinical variables, the panelists had much less importance as a determinant of ratings than such factors as severity and stability of anginal symptoms, non-invasive test results, or stenosis of major coronary arteries. In contrast, when Goyert, *et al*, examined practices of 11 obstetricians at a single hospital, only nulliparity exceeded practitioner identity as a risk factor for operative delivery.[15]

The revascularization panel's underlying agreement about determinants of urgency proved sufficient to permit a consensus on general principles governing triage of this patient population when the panelists convened in January 1989.[16] These guidelines are already being applied in a pilot Toronto program, were presented to a province-wide conference in November 1989, and will be undergoing further review by a multi-center working party during 1990. The ultimate goal is to standardize triage criteria voluntarily across the province so that inter-practitioner and inter-institutional discrepancies in waiting times can be reduced in the interests of fairness and efficiency.

ACKNOWLEDGMENTS

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APPENDIX A

Expert Panel of Cardiologists and Surgeons

Ronald S. Baigrie, MD, Chief of Cardiology, Sunnybrook Medical Center, Associate Professor, Department of Medicine, University of Toronto (Co-chairman).

Donald S. Beanlands, MD, Deputy Director, University of Ottawa Heart Institute, Professor, Department of Medicine, University of Ottawa.

Neil Berman, MD, Cardiologist, Toronto Hospital, Associate Professor, Department of Medicine, University of Toronto.

David Borts, MD, Cardiologist, Peel Memorial Hospital, Brampton, Ontario.

John A. Cairns, MD, Cardiologist, Hamilton General Hospital, Professor and Chairman, Department of Medicine, McMaster University, Hamilton (Co-chairman).

David H. Fitchett, MD, Cardiologist, Montreal Heart Institute, Associate Professor, McGill University, Montreal.

Bernard S. Goldman, MD, Chief of Cardiovascular Surgery, Sunnybrook Medical Center, Professor, Department of Surgery, University of Toronto (Co-chairman).

John Gunstensen, MD, Cardiovascular Surgeon, Hamilton General Hospital, Professor, Department of Surgery, McMaster University.

Amin Haq, MD, Cardiologist, Toronto Hospital, Associate Professor, Department of Medicine, University of Toronto (deceased).

Allan Hess, MD, Cardiologist, York County Hospital, Newmarket, Ontario.

William Hughes, MD, Cardiologist, Peterborough Civic Hospital, Peterborough, Ontario.

Samuel V. Lichtenstein, MD, Cardiovascular Surgeon, St. Michael's Hospital, Assistant Professor, Department of Surgery, University of Toronto.

David Salter, MD, Cardiovascular Surgeon, Toronto Hospital, Assistant Professor, Department of Surgery, University of Toronto.

James Swan, MD, Cardiologist, Scarborough Centenary Hospital, Scarborough, Ontario.

Allan Tinmouth, MD, Cardiologist, Scarborough General Hospital, Scarborough.

Richard D. Weisel, MD, Cardiovascular Surgeon, Toronto Hospital, Associate Professor, Department of Surgery, University of Toronto.

APPENDIX B

Factors and Levels Adopted by the Cardiology Panel for Patient Triage

A. Presenting pain syndrome and therapeutic response

1. Stable angina on reasonable medical therapy: mild to moderate [Canadian Cardiovascular Society classes I-II][17]
2. Stable angina on reasonable medical therapy: severe [Canadian Cardiovascular Society class III.][17]
3. Unstable angina, pain resolved with intensified medical therapy, and now on oral medication.
4. Unstable angina, symptoms improved but angina with minimal provocation.
5. Symptoms persisting or hemodynamically unstable, requiring coronary care monitoring and parenteral medication.

B. Coronary anatomy defined by angiography

1. Left main coronary artery stenosis with or without other stenoses.
2. Two or three vessel disease, *including* the proximal left anterior descending [LAD] artery or equivalent.
3. Three vessel disease *without* involvement of the proximal LAD artery.
4. Single vessel disease involving the LAD or equivalent vessel.
5. Single or two vessel disease *without* a proximal lesion of LAD artery or an equivalent vessel.

C. Expected procedural morbidity and mortality

1. High (e.g., renal failure, diabetes, peripheral vascular disease, chronic obstructive airways disease).
2. Average/Low

D. Reversible ischemia on non-invasive tests

1. *High risk:* e.g. poor performance on treadmill testing, with early and unequivocal ST-segment changes on electrocardiogram; thallium defects on exercise or dipyridamole stress testing involving either an extensive portion of the anterior wall or multiple areas.
2. *Low* risk: any test failing to meet the above criteria.

E. Left ventricular ejection fraction

1. >50%, approximately grade 1
2. 30/35%–50%, approximately grade 2
3. 20%–30/35%, approximately grade 3
4. <20%, approximately grade 4

F. Previous CABS: Yes/No

G. Myocardial infarction within previous 4 weeks: Yes/No

APPENDIX C

Urgency/Appropriateness Rating Scale Accepted by the Expert Cardiology Panel

1.	Emergency	Immediate revascularization
2.	Extremely urgent	Within 24 hours
3.	Urgent	24–72 hours
4.	Semi-urgent	72 hours to 14 days (same admission)
5.	Short list	2 weeks to 6 weeks
6.	Delayed	6 weeks to 3 months
7.	Marked Delay	3 months to 6 months
8.	Questionable if revascularization should be undertaken	
9.	Inappropriate for revascularization to be undertaken	

Note: Each urgency rating level represents the period within which revascularization is expected to be performed; the outer time limit for each limit represents the maximum acceptable waiting period for patients assigned that urgency rating.

APPENDIX D

Calculation of Agreement Indices

The agreement index was determined as in Davies and Fleiss[7] to calculate the probability that two panelists chosen randomly (without replacement) would agree on the rating of any scenario chosen with equal probability from all possible scenarios.

Thus, the $\binom{16}{2}$ pairings of raters were assessed for agreement on each scenario. Agreement was defined as either strict agreement on urgency scale, or agreement on the clinical categories "DO", "WAIT", and "NOT" (see text for definitions).

Hence, if $I_n(r_1, r_2) = 1$ for r_1 and r_2 agreeing on scenario "n" and 0 otherwise, then:

$$P_a = \frac{\sum_{n} \sum_{r_1<r_2} I_n(r_1, r_2)}{n\binom{16}{2}}$$

Note that "chance agreement" between two panelists is possible. This is calculated as

$$P_c = \frac{\sum_{j} \sum_{r_1<r_2} P_j(r_1)\, P_j(r_2)}{\binom{16}{2}}$$

where $P_j(r)$ is the marginal probability that the rating of panelist "r" is "j".

Thus, $P_k = \frac{Pa - P_c}{1 - P_c}$ is the chance corrected, or "kappa" agreement.

Note that kappa may be calculated either for each chapter or over all the scenarios, irrespective of chapter. The variance of the agreement indices is readily calculated and computed, but is unwieldy. (Available on request to author.)

Patient, Provider and Hospital Characteristics Associated with Inappropriate Hospitalization

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Abstract: To determine the relation between patient and provider characteristics and inappropriate hospital use, we examined adult nonpregnancy hospitalizations from a randomized trial of health insurance conducted in six sites in the United States. Appropriateness of inpatient treatment was based on medical record review; patient characteristics on sociodemographic, economic, and health status; and provider characteristics on descriptors of physician practice and hospital facilities.

Twenty-seven percent of admissions attended by physicians licensed for more than 15 years were judged inappropriate, compared to 20 percent for younger physicians. Admissions were more likely to be inappropriate if the patient was female (27 percent compared with 18 percent). Controlling for patient and provider characteristics reduces but does not eliminate the differences in the appropriateness of inpatient care across the study's six sites. Differences in available provider and patient characteristics do not account for geographic differences in inappropriate hospitalization in this study. (*Am J Public Health* 1990; 80:1253–1256.)

Introduction

As part of a wider concern for health care cost containment, recent attention has focused on the inappropriate use of hospital care. Recent studies have documented substantial inappropriate hospital use for adults, as well as children.[1–5] In the RAND Health Insurance Experiment, we reported previously that 23 percent of the admissions made inappropriate use of the acute hospital setting or level of care, while an additional 17 percent of admissions were avoidable by use of ambulatory surgery.[2] In this report, we examined the effect of patient, physician, and hospital variables on inappropriate hospitalizations and days. Our data provide some of the most detailed and comprehensive information available on the health status of patients.

Methods

The health insurance experiment was a randomized trial of cost sharing in health insurance conducted in six United States sites. Families entered the experiment between 1974–77 and were assigned to one of 14 different fee-for-service health insurance plans with different levels of cost sharing. The experiment excluded persons 62 years of age and older at the time of enrollment, those with incomes in excess of $25,000 in 1973 dollars, those eligible for Medicare disability, those in the military and their dependents, veterans with service-connected disabilities, and individuals imprisoned or institutionalized. Additional details on the design of the Health Insurance Experiment are available elsewhere.[6,7]

The sample of 3,413 individuals used as a basis for this analysis includes all enrollees who were 18 years of age or older at enrollment into the study. Medical records were obtained from 90 percent of the hospitalizations for these individuals. We excluded admissions for labor and delivery, psychiatry, and alcohol rehabilitation. This resulted in a sample of medical records from 1,132 admissions.[2]

To determine the appropriateness of hospital admissions or hospital days, two board-certified physicians reviewed medical records using the Appropriateness Evaluation Protocol.[3,8] They classified each admission or randomly selected hospital day into one of three categories: appropriate, inappropriate, or avoidable by ambulatory surgery. In this report, however, we considered admissions avoidable by ambulatory surgery as appropriate for two reasons. Ambulatory surgery centers were not available in all sites during the study period. Further, in Siu, *et al*,[2] the findings were not sensitive to whether ambulatory surgery was considered appropriate or inappropriate. Additional details on the review of hospital records for appropriateness are available elsewhere[2] or on request to the authors.

We use four groups of variables to explain the variation in inappropriate inpatient care: insurance plan, patient health status, patient sociodemographic and economic measures, and provider characteristics. We group the insurance plans into three groups: 1) the free plan (no out-of-pocket cost to the family); 2) the family cost sharing or pay plan, where the coinsurance rate is 25–95 percent for all services up to an upper limit on out-of-pocket expenses; and 3) the individual deductible plan with a 95 percent coinsurance rate for outpatient services (subject to an out-of-pocket limit) and free inpatient care. We use three measures of health status: 1) general health perceptions; 2) physical or role limitations; and 3) chronic disease status. Each measure is based on the self-administered Medical History Questionnaire completed at the beginning of the study. The General Health Index measures perceptions of overall health, as well as resistance to illness and health worry.[9,10] The physical or role limitations measure is scored dichotomously (1 = limited, 0 = otherwise) to indicate the presence of one or more limitations in self-care, mobility, physical activity, and usual role activities; the chronic disease measure is a simple count of the number of diseases or health problems.[11–14] The model used in our analysis also includes covariates for study site, patient age, sex, race, education, and family income and size. With the exception of family income, the data were collected before or at enrollment in the study (1974–77). Family income data are from 1975 in Dayton, 1978 for the three-year group in South Carolina, and 1976 for all other participants.

Variables describing the hospitals were obtained from the American Hospital Association files. This included information regarding accreditation, the presence of a residency program, medical school affiliation, ownership, number of beds, number of admissions, occupancy rate, and available facilities. Information on attending physicians was

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obtained from the American Medical Association Directory of Physicians' Master File. For osteopaths, we obtained information from the Directory of the American Osteopathic Association. We located 95 physicians missing from these two sources by way of the computerized National Yellow Pages. For this latter sample of physicians, information on their characteristics was obtained from their practices by phone interview. These sources yielded information on physician sex, years from licensing, type of practice, practice arrangement, self-designated specialties, and board certification.

Although we obtained patient and hospital descriptors on all 1,132 admissions for whom medical records were available, some information is missing: nine percent for specialty, 12 percent for licensing, and 19 percent for solo/group practice data. Missing data were replaced by the mean value for that variable in regressions, and dummy variables were included to indicate cases with data missing for a given variable. The Appendix lists the independent variables used in this analysis and their means.

Statistical Methods

We used a logistic regression to estimate the probability that a particular admission or hospital day was medically inappropriate. The dependent variable in these regressions is whether the admission or day is inappropriate. For different groups (e.g., site, sex, specialty), we make both unstandardized and standardized comparisons. For the unstandardized comparisons, we predict the mean probability (and calculate its standard error) without correcting for the other differences between the contrast groups. For example, in comparing Seattle with one of the rural sites, we do not adjust for the differences in the mix of physicians or hospital types. We also estimate standardized predictions that remove the effects of factors confounded with the contrast of interest. For example, we want to purge the Seattle-rural site comparison of differences in patient and provider mix. To do this, we predict the probability that each admission or day is inappropriate if that case were in Seattle, then as if it were in Dayton, etc. This procedure is like the usual direct adjustment, except that it is based on the estimated model that controls for several factors simultaneously. All inference statistics are corrected for intratemporal correlation, as well as correlation among providers and family members.[15] We report standardized predictions and 95 percent confidence intervals (CI) for differences between categories of independent variables; p-values are reported in the text for the overall effect of statistically significant independent variables with multiple categories.

Results

As previously reported, we found that 23 percent of the adult hospital admissions were inappropriate and 35 percent of the days were inappropriate.[2] Logistic regression with hospital admission inappropriateness as the dependent variable showed that cost-sharing had no effect on the proportion of admissions that were inappropriate. However, there were differences by site ($p = 6.2 \times 10^{-5}$), gender, education ($p = 0.03$), hospital accreditation and bed size, and physician specialty ($p = < 10^{-8}$) and length of time since licensing.

Unstandardized estimates showed that a greater likelihood of an inappropriate hospital admission was associated with a number of variables, but these differences could be due to the intrinsic differences among the groups compared or to other factors that differ among the groups. The standardized comparisons control for these other differences. The standardized predictions in Table 1 demonstrate that the proportion of admissions considered inappropriate are increased substantially if the physician was licensed more than 15 years ago or if the patient was female, and increased moderately if the attending physician was either an internist or a general/family practitioner.

Logistic regression showed that cost sharing had no effect on the appropriateness of a hospital day. Site differences persisted ($p = 0.03$) although they were smaller. Among the patient variables, only sex remained associated, and none of the hospital variables remained associated; years from licensing remained associated among the set of physician variables.

For unstandardized comparisons, the likelihood of a hospital day being inappropriate is increased if the physician was not board certified or was licensed more than 15 years ago, if the hospital was nonpublic, and if the patient was female. The standardized estimates (Table 2) are similar to those for inappropriate admissions although years from licensing and patient gender are more strongly associated and physician specialty less strongly associated.

There were substantial unstandardized differences across sites in the inappropriate use of inpatient care. In the case of both hospital admissions and days, the lowest proportion of inappropriate use is found in Seattle. Standardizing for patient, physician, and hospital variables reduced but did not eliminate the variation among sites in inappropriate use (Table 3). Addition of these explanatory variables reduced the variation resulting from site differences from 5.1 percent to 2.6 percent for hospital admissions and from 2.4 percent to 1.6 percent for inappropriate days. This is most

TABLE 1—Inappropriate Admissions by Provider and Patient Characteristics

Characteristics	Standardized Percentage	Difference (95 % CI) versus Initial Category
Specialty		
General/family	33.8	—
Internal Medicine	34.0	0.2 (−10.1, 10.5)
Surgery	17.3	−16.5 (−25.7, −7.3)
Obstetrics/gynecology	8.1	−25.7 (−34.6, −16.8)
Solo Practice		
Yes	23.2	—
No	23.2	0.0 (−6.3, 6.3)
Board-Certified		
Yes	21.4	—
No	27.5	6.1 (−1.1, 13.2)
Years from Licensing		
≥15	26.8	—
<15	20.0	−6.8 (−12.8, −0.8)
JCAH Accredited		
Yes	21.9	—
No	32.4	10.5 (−0.4, 21.4)
Teaching Status		
Yes	24.0	—
No	22.9	−1.1 (−11.5, 9.3)
Public Hospital		
Yes	20.9	—
No	23.3	2.4 (−9.4, 14.2)
Sex		
Male	17.8	—
Female	26.8	9.0 (4.6, 13.4)
Education		
High School	36.7	—
<High School	36.5	−0.2 (−8.4, 8.1)
Some College	29.4	−7.3 (−17.9, 3.3)
College	27.7	−9.0 (−21.2, 3.3)

TABLE 2—Inappropriate Days by Provider and Patient Characteristics

Characteristics	Standardized Percentage	Difference (95% CI) versus Initial Category
Specialty		
General/family	39.7	—
Internal Medicine	36.6	−3.1 (−14.9, 8.7)
Surgery	30.0	−9.7 (−20.3, 1.0)
Obstetrics/gynecology	33.3	−6.4 (−19.8, 7.1)
Solo Practice		
Yes	34.4	—
No	32.4	−2.0 (−10.6, 6.5)
Board-Certified		
Yes	31.6	—
No	39.2	7.6 (−1.0, 16.3)
Years from Licensing		
≥15	39.0	—
<15	29.9	−9.1 (−17.0, −1.2)
JCAH Accredited		
Yes	33.7	—
No	41.2	7.5 (−6.6, 21.6)
Teaching Status		
Yes	36.5	—
No	33.9	−2.6 (−16.3, 11.0)
Public Hospital		
Yes	30.3	—
No	34.9	4.6 (−10.9, 20.0)
Sex		
Male	23.5	—
Female	42.0	18.5 (10.9, 26.1)

TABLE 3—Inappropriate Hospital Use by Site

	Admissions		Days	
Site	Standardized Percentage	Difference (95% CI) vs Initial Category	Standardized Percentage	Difference (95% CI) vs Initial Category
Seattle	11.4	—	22.1	—
Dayton	20.3	8.9 (0.1, 17.7)	45.7	23.7 (9.2, 38.1)
Fitchburg	17.4	6.0 (−2.2, 14.3)	33.6	11.5 (−2.3, 25.3)
Franklin	24.2	12.8 (3.7, 22.1)	39.2	17.1 (4.5, 29.8)
Charleston	30.8	19.4 (8.5, 30.5)	34.4	12.3 (−2.3, 27.0)
Georgetown	34.4	23.0 (13.7, 32.4)	34.0	11.9 (0.2, 23.7)

striking in the comparison of Georgetown and Seattle for hospital days, where a twofold unstandardized difference (42 compared with 21 percent; not shown) in inappropriate days was reduced by half (34 compared with 22 percent). Thus, although addition of patient, physician, and hospital variables decreased the extent of variation, significant geographic differences in the proportion of inappropriate hospital use remain even after controlling for these sources of variation with available variables.

Discussion

The sites in this study differed in patient characteristics and in provider types and availability, and we found that some of these characteristics were associated with inappropriate use. Nevertheless, we found that site differences in the proportion of inappropriate hospital use remain, even after controlling for most measurable aspects of patient, provider, and hospital characteristics. This finding confirms, for inappropriate hospital use, Wennberg's observation that practice patterns differ by geographic region and cannot be fully explained by geographic differences in patient or provider characteristics.[16]

The magnitude of these site differences was reduced by controlling for these patient and provider variables, some of which were strongly associated with inappropriate use. For both hospital admissions and days, we found that older physicians and female patients were more likely to be associated with inappropriate use. Although certain physician specialties were less likely to result in an inappropriate admission, these specialty differences in inappropriate use were most likely related to the performance of procedures. Many patients admitted by surgeons and gynecologists underwent a procedure within the first day of admission, leading the hospitalization to have been more likely designated appropriate for acute level care.

We cannot determine whether the effect of years from licensing is related either to declining clinical skills or to a cohort effect. Similarly, we are unable to explain the gender differences in inappropriate hospitalization. Gender effects have been observed in most studies attempting to explain overall patterns of medical care utilization.[17] The differences observed in our study could not have been due to child bearing, because pregnancy and related admissions were excluded from this analysis. This leaves a number of possible explanations, including differences in (a) how physicians perceive women's health needs, (b) the level of support available to women at home, and (c) the types of nonobstetric medical problems encountered by women.

Our results reaffirm the importance and policy significance of geographic variations in medical practice. The geographic variations observed in this study could not be attributed solely to patient and provider characteristics, many of which are difficult to modify. Future research should focus on the identification of modifiable variables and methods to reduce inappropriate hospital use.

Current cost containment policies are not likely to selectively reduce inappropriate hospital use,[2] and other approaches to do so are necessary. Retrospective review with feedback of results to physicians[18] may be one such approach. Conducting retrospective audits and making these results available to major buyers (e.g., major employers) is another approach to this problem. While it would be more efficient to target such reviews on those hospitalizations most likely to be inappropriate, our results suggest that targeting to specific physicians or hospitals on the basis of various characteristics would be very difficult. To reduce inappropriate hospital use by mechanisms involving targeted utilization review, other approaches to targeting will need to be developed.

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APPENDIX
Sample Characteristics

Variable	Mean (standard deviation) or percent
Patient Characteristics	
Age (years)	42.2 (12.2)
% Female	60
% Black	15
% receiving AFDC	5
General health index	62.9 (16.7)
Mental health index	72.8 (14.6)
% with role or physical limitation	36
% on cost sharing plan	39
% on individual deductible plan	22
Log (family size)	1.05 (0.55)
Log (family income)	8.77 (0.70)
% with <12 years of education	35
% with 12 years of education	39
% with >12 years of education	26
Physician Characteristics	
% solo practitioner	45
% board-certified	66
% in internal medicine	21
% in surgery	43
% in obstetrics/gynecology	13
% in general or family practice	18
% in licensed for ≥15 years	51
Hospital Characteristics	
% JCAH approved	89
% belonging to Council of Teaching Hospitals or having an AMA approved residency	26
% public hospitals	9
Log (bedsize)	5.41 (0.63)

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Public Health Briefs

Surveillance of Occupational Lung Disease: Comparison of Hospital Discharge Data to Physician Reporting

KENNETH D. ROSENMAN, MD, LINDA TRIMBATH, AND MARTHA STANBURY, MPH

Abstract: A survey of 762 New Jersey physicians showed that 35% reported seeing patients with either asbestosis, coal worker's pneumoconiosis, occupational asthma or silicosis. Three to four times as many patients with these diagnoses were seen as outpatients as were hospitalized. The implications of these results in using hospital discharge data for occupational disease surveillance are discussed. (*Am J Public Health* 1990; 80:1257–1258.)

Introduction

It has been proposed that hospital discharge data be used as part of an occupational disease surveillance system.[1,2] One of the limitations of hospital discharge data is the lack of information on non-hospitalized individuals. We conducted a survey of physicians in New Jersey to obtain estimates of how many patients they saw in their practice with asbestosis, coal workers' pneumoconiosis, occupational asthma, or silicosis in comparison to the number of patients they admitted to the hospital with the same diagnosis.

Methods

The names and addresses of physicians were obtained either from the state hospital discharge system or directly from the hospitals under state occupational disease reporting regulations (New Jersey Administration Code 8:57–1.13). Names and addresses of physicians were obtained by linking medical license numbers in the hospital discharge record to a data set of all licensed physicians in the state. The physicians surveyed had discharged at least one patient for the year 1985, 1986 or 1987 from one of New Jersey's 105 acute care (non-federal) hospitals with the diagnosis of asbestosis (ICD 501), coal workers' pneumoconiosis (ICD 500), pneumoconiosis due to other inorganic dust (ICD 503), pneumonopathy due to inhalation of other dust (ICD 504), pneumoconiosis unspecified (ICD 505), silicosis (ICD 502).

In the spring of 1988, a letter was mailed to these physicians requesting information about their medical specialty, an estimate of the total number of their patients newly diagnosed with asbestosis, coal workers' pneumoconiosis, occupational asthma, and silicosis in the calendar year 1987, and an estimate of the proportion of these patients admitted to the hospital during that same year. Non-respondents to a second and third mailing were contacted by telephone.

Results

A total of 847 physicians were included in the survey, of whom 762 (90.0 percent) completed the questionnaire. The reasons for non-response were: 29 (3.4 percent) letters were undeliverable; 20 (2.4 percent) refused to participate when telephoned; 11 (1.3 percent) were unreachable despite five telephone calls; nine (1.1 percent) had unlisted telephone numbers; six (.7 percent) retired; five (.6 percent) moved out of state; five (.6 percent) were deceased.

Table 1 shows the number of respondents, by medical specialty, who saw patients in 1987 with any of the lung conditions under consideration. The percentage of physicians reporting patients in 1987 is less than 100 percent, because many physicians may have had no patients with these diagnoses in 1987 or because they did not report all such patients.

Table 2 shows the proportion of patients hospitalized: for asbestosis 34 percent (95% CI = 31, 37); for coal workers' pneumoconiosis 26 percent (95% CI = 18, 35); for occupational asthma 23 percent (95% CI = 19, 27); for silicosis 27 percent (95% CI = 20, 35) were hospitalized. For all diseases combined, 548 (30 percent) of 1,814 patients (95% CI = 28, 32) were hospitalized.

Discussion

For the four diseases surveyed, physicians stated that for every patient hospitalized with the condition they had two to three additional patients with the same diagnosis who had not been hospitalized. This selected group of physicians reported nearly as many newly diagnosed cases of pneumoconiosis in New Jersey as are reported annually in the supplementary data system of the Bureau of Labor Statistics.[4] The number of additional patients not hospitalized varied both by disease as well as by the specialty of the reporting physician. The variation of hospitalization by specialty may be a reflection of the severity of disease seen by different physicians. For example, surgeons reported that 79 percent of their patients with asbestosis were hospitalized. The variation, however, may also reflect the relative amount of time physicians see hospitalized versus ambulatory patients.

None of the physicians reported their specialty as occupational medicine. Hospitalizations were not limited to a few specialty groups such as pulmonary physicians. Percentages of physicians reporting patients with lung conditions in 1987 by specialty varied from 8–79 percent although all physicians had admitted patients with these lung conditions

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TABLE 1—Total Number of Physicians Responding and Percent by Specialty who Reported Patients for the year 1987 with Either Asbestosis, Coal Workers' Pneumoconiosis, Occupational Asthma, or Silicosis

Medical Specialty	Number Physicians Responding	Percent Physicians Reporting Patients with Any of the Lung Conditions	Percent Physicians Reporting Asbestosis	Percent Physicians Reporting Silicosis	Percent Physicians Reporting Coal Workers' Pneumoconiosis	Percent Physicians Reporting Occupational Asthma
Internal Medicine	205	43.9	33.2	8.8	6.3	18.5
Pulmonary	65	78.5	70.8	29.2	30.8	61.5
Family/General Medicine	106	41.5	30.2	7.5	9.4	20.9
Surgery	110	17.3	16.4	3.6	0.9	2.7
Cardiology	80	35.0	31.3	3.8	6.3	10.0
Urology	49	8.2	8.2	0.0	0.0	0.0
All Other Specialties	126	18.3	14.3	1.6	4.0	16.7
No Specialty	21	19.0	14.3	4.8	0.0	4.8
Total	762	34.5	28.1	7.2	7.1	17.6

TABLE 2—Numbers of Reported Patients and Percent Hospitalized in 1987 with each Occupational Lung Disease by Physician Specialty

	Asbestosis		Silicosis		CWP		Occup Asthma		All Lung Diseases	
Physician Specialty	No. pts	% hosp	No. pts	% hosp	No. pts	% hosp	No. pts	% hosp	No. pts	% hosp
Internal Medicine	162	45	33	46	27	37	138	24	360	36
Pulmonary	592	17	66	26	46	15	188	20	892	19
Fam/Gen Medicine	78	32	15	7	11	36	61	13	165	23
Surgery	77	79	15	0	1	0	16	19	109	59
Cardiology	140	61	16	4	12	25	21	62	189	57
Urology	5	20	0	—	0	—	0	—	5	20
All other specialties	53	55	4	25	6	50	21	29	84	46
No specialty given	8	25	1	0	0	—	1	0	10	20
Total	1115	34	150	27	103	26	446	23	1814	30

in 1985, 1986 or 1987. Efforts are underway to follow up this survey by encouraging the physicians to report the names of patients they estimated on the questionnaire. Similar surveys in other states will be useful to examine if there are differences in care patterns in different states.

The physicians response rate to the questionnaire was excellent. We attribute this to its briefness and to our only asking for estimates. This is also its major limitation as we did not evaluate the accuracy of the physicians estimates. According to statewide hospital discharge data for 1986, there were 881 patients discharged with asbestosis, 97 patients with silicosis, and 235 patients with coal workers' pneumoconiosis. For the first two diagnoses, the hospital discharges were less than those reported by the physicians; for coal workers' pneumoconiosis, the hospital discharges were more than those reported by physicians. No data on occupational asthma is available from discharge data.

If the percentages of underreporting of 67 to 75 percent for different diseases found in this survey is generalizable and reassessed by periodic surveys of physicians then hospital discharge data because of its relative ease of collection and low cost would be a useful method to examine trends and estimate the number of occupational pneumoconioses.

Recently, the National Institute for Occupational Safety and Health (NIOSH) has been promoting the concept of sentinel provider-based occupational disease surveillance systems.[3] This survey shows that hospital discharge data can be used directly or indirectly to identify names, addresses and medical specialties of potential sentinel providers, and that, with sufficient follow-up, these physicians are willing to report to a state health department information that can be relied on for occupational disease surveillance.

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Food-borne Outbreak of *Giardia Lamblia*

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AND WILLIAM PARKIN, DVM, DRPH

Abstract: An outbreak of giardiasis occurred following a family party for 25 persons. Nine who had eaten fruit salad became ill, compared with one who had not eaten the salad (Relative Risk = 7.4, 95% CI = 1.4, 169.3). The fruit salad preparer had a diapered child and a pet rabbit at home who were both positive for *Giardia lamblia*. This outbreak emphasizes the importance of good hygienic practices in food preparation and the possibility of domestic-animal-to-person transmission in *Giardia* outbreaks. (*Am J Public Health* 1990; 80:1259–1260.)

Introduction

Giardia lamblia infection is often acquired by drinking contaminated water[1,2] or by person-to-person transmission among preschool children.[3] Transmission by food was first reported in 1981 when an outbreak of giardiasis was caused by eating contaminated home-prepared salmon.[4] We report an outbreak of giardiasis which most likely occurred due to the contamination of a fruit salad with *Giardia* cysts. The investigation also raises the question of whether domestic animals can play a part in transmission.

Background

On March 30, 1986, a party for 25 persons from seven separate family groups was held at a private home in southern New Jersey. Within seven days of the party, several attendees developed giardiasis. The outbreak was identified by the county health department from seven stool specimens received from ill attendees which were positive for *G. lamblia*.

Methods

All party attendees were contacted by telephone, and a questionnaire was administered. Guests were asked whether they had had a diarrheal illness, which of 30 possible food and drink items they had consumed at the party, and whether they had been in contact with day care centers or institutions for the handicapped. To determine if there was a widespread outbreak of giardiasis in the area, four local hospitals were contacted.

A case of giardiasis was defined as a person who had diarrhea (>3 stools/day) for >5 days with or without fever, *or* intermittent diarrhea >5 days (with or without fever) with two or more of the following symptoms: flatulence, nausea, malaise, or abdominal cramps.

Stool specimens were collected from all party attendees and from the children and staff at the local babysitting service which was attended by a diapered child who had been at the party. Specimens were examined for *Giardia* microscopically and enteric bacterial cultures were performed for *Salmonella*, *Shigella*, and *Campylobacter* on all persons with clinical symptoms. A stool specimen was also obtained from a pet rabbit in the home of the diapered child and examined for *Giardia* cysts.

The environmental investigation included an account of the preparation of the food and an investigation of the household water supplies using filters.

Results

Epidemiology

Ten cases of outbreak-associated giardiasis were identified. Nine (eight stool positive) of the cases had onset of symptoms during the period six to 12 days following the party and one case (stool negative) occurred 18 days after the party. Three community giardiasis cases were reported from the local hospitals for the previous five months.

Attack rates by gender and age groups were similar; each household had at least one member who was a case (Table 1). The attack rate for 20 persons who had eaten some food at the gathering was 50 percent compared to zero for those not eating. The five persons who had not eaten any food were excluded from further consumption analysis. Among those eating food at the party, those eating fruit salad were seven times more likely to have a case of illness than those who did not eat the salad (82 percent, 9/11 vs 11 percent, 1/9, RR = 7.4, 95% CI = 1.4, 169.3) (Table 2); nine of the 10 case-patients and all of the stool-positive cases had eaten fruit salad.

Laboratory

Stool specimens from eight of the 10 case-patients were positive for *G. lamblia;* all were negative for enteric bacterial pathogens. One of the two cases with negative studies for *Giardia* had been on metronidazole for 10 days.

Environmental

The fruit salad was prepared in the home of a woman who became ill nine days after the party. She had a two-year-old diapered child who, with four other children, was cared for by a babysitter during the day. Her child, who had eaten the fruit salad, had had no symptoms of gastroenteritis but had a positive stool for *Giardia* on the first specimen. The

TABLE 1—Family Attack Rates among Party Attendees, *Giardia* Outbreak, New Jersey, 1986

Family	Number Persons	Number Cases	Number Stool Positive
A	4	2	2
B	2	2	2
C	4	1	2
D	5	1	0
E	5	1	1
F	2	2	2
G	3	1	0
Total	25	10	9

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TABLE 2—Food-Specific Attack Rates (AR), *Giardia* Outbreak, New Jersey, 1986

	Ate Food	Did Not Eat Food	
Food Item*	Case/Total AR (%)	Case/Total AR (%)	RR (95% CI)
Cold Foods			
Ham	7/13 (54)	3/7 (43)	1.3 (0.5.5.2)
Corned Beef	6/9 (67)	4/11 (37)	1.8 (0.6,4.7)
Deviled Eggs	8/15 (53)	2/5 (40)	1.3 (0.5,9.7)
Potato Salad	6/8 (75)	4/12 (33)	2.3 (0.8,4.8)
Coleslaw	7/11 (64)	3/9 (33)	1.9 (0.6,7.0)
Bread	6/8 (75)	4/12 (33)	2.3 (0.8,4.8)
Rolls	7/13 (54)	3/7 (43)	1.3 (0.5,5.2)
Drinks			
Sodas	7/12 (58)	3/8 (38)	1.5 (0.5,6.2)
Deserts			
Fruit Salad	9/11 (82)	1/9 (11)	7.4 (1.4,169.3)

*Only foods eaten by >50% of the case-patients are reported.

four other children attending the babysitter's home and the babysitter's family were negative for *Giardia*.

Two days before the party, this diapered child had been given a pet rabbit as a present. The animal had been present in the kitchen when the fruit salad was being prepared. The rabbit was positive for *Giardia* (unspecified).

The salad was made two to three hours before being served. The fruit was either peeled or cut on a lucite chopping board and then placed in a plastic bowl with a lid.

No *Giardia* cysts were found in the filters from the homes.

Discussion

This outbreak of giardiasis represents a point-source outbreak with the fruit salad as the most likely vehicle of transmission. The high attack rate for those persons who ate the salad (82 percent, 9/11) implies that *Giardia* was effectively transmitted by this food.

The outbreak had some similarities with the salmon outbreak previously reported.[4] Both had high attack rates for persons who ate the contaminated food—48 percent for salmon and 82 percent for fruit salad—and, in both outbreaks, food was probably prepared without prior hand washing. Diapered infected children were present in both homes where the contaminated food was prepared.

There are two likely hypotheses for transmission of *Giardia* and both postulate that the fruit salad was contaminated by the food preparer who had failed to wash her hands before food preparation. The first hypothesis is that changing of the infected child's diaper would have been an effective way of transmitting cysts to a persons' hands and then to the fruit salad. Fruit salad contains a liquid acid medium which would maintain the viability of *Giardia* cysts which are known to be resistant to acid.[5] It is also known that cysts are rapidly destroyed when dried, but remain viable for weeks under moist conditions.[6]

The second hypothesis for transmission is that the rabbit was positive for *Giardia* when it entered the home and was excreting cysts. These cysts were transferred to the hands of the food preparer who contaminated the fruit salad by failing to wash her hands. There is one report of an outbreak of giardiasis in which transmission occurred between animals and humans in a zoo.[6] In addition, there has been a report that suggests that cats may be responsible for introducing giardiasis into households[7] but little is known about the importance of animals as reservoirs of the human *Giardia*[6] or the susceptibility of humans to animal *Giardia* (other than *G. lamblia*). Traditionally it has been believed that *Giardia* is highly host-specific.[8]

We recommend that when health department personnel investigate *Giardia* outbreaks, they should consider the possibility of food-borne transmission and when giardiasis occurs in a household that contains domestic animals, stool specimens should be collected from the animals for cyst microscopy. If possible, the human and animal species of *Giardia* should be determined. In this way, more information will be collected to determine if *Giardia* cysts are transmitted between domestic animals and humans.

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Leukemia Incidence and Radioactivity in Drinking Water in 59 Iowa Towns

LAURENCE FUORTES, MD, LOUISE ANN MCNUTT, MS, AND CHARLES LYNCH, MD, PHD

Abstract: Fifty-nine towns in Iowa with single source drinking water supplies were stratified on the basis of radium content in finished non-softened water to test the hypothesis of an association with total or acute myeloid leukemia. Fourteen towns had radium concentrations in drinking water exceeding the EPA safety limit of 5 picocuries per liter (pCi/L). A small increasing trend existed for total leukemia with increased radium content in drinking water that is in accordance with either the hypothesis of no effect or of a small effect. (*Am J Public Health* 1990; 80:1261–1262.)

Introduction

Several studies have documented increased cancer incidence or mortality associated with radioactivity of drinking water. The US Environmental Protection Agency (EPA) has set a safety limit of 5 picocuries per liter (pCi/L) for total radium in public water supplies. There are a number of communities nationwide whose water supplies exceed this limit. In a study reported in 1966 on low level radium 226 exposure, death rates from bone cancer were found to be higher in municipalities exposed to higher levels of radium 226 in drinking water. The numbers of cases were small, however.[1]

Ingested radium (Ra^{226} and Ra^{228}), an alpha particle emitter, is a well documented cause of bone and nasal cancers in studies of radium dial painters and follow-up of patients treated with Ra^{224}. In the radium dial painters, the risk of developing bone cancer was impressive in magnitude, (RR = 50), and specific to bone.[2] In the studies of human subjects treated with Ra^{224} (a shorter lived isotope), the risk of both bone cancers and leukemias was increased.[3]

A recent study from Florida revealed an association of acute myelogenous and total leukemia incidence rates with radium content in private wells. In that study, 27 counties were chosen based on their proximity to deposits of phosphate ore.[4] Based on a survey of 50 private wells in each county, 10 counties had high exposure and 17 had low exposure. Counties with greater than 5 pCi/L of radium in 10 percent or more of the sampled wells were included in the high exposure group. The age-standardized incidence density ratio for high exposure vs low exposure was 1.49 for total leukemia and 2.00 for acute myelogenous leukemia.

In a previous Iowa study, associations of radioactivity in drinking water were reported with lung, breast, and bladder cancer.[5] The Iowa data were reexamined in an attempt to determine if radioactivity in drinking water was associated with leukemia incidence.

Methods

Fifty-nine Iowa towns, each of less than 10,000 population, with a single source water supply and without water softening in their treatment process were identified from an Iowa Geologic Survey Bureau data base. The towns were stratified into three groups according to radium^{-226} content in finished water: *high* = Ra^{-226} greater than 5 pCi/L, *medium* = Ra^{-226} between 2–5 pCi/L, and *low* = Ra^{-226} less than 2 pCi/L. For each of the towns studied, there were greater than 2 radium measurements in finished water available. By this schema there are 812,616 persons years in the high, 2,055,060 in the middle, and 1,562,652 person years in the low exposure categories.

Identification of leukemia cases was performed by the State Health Registry of Iowa. Cancer incidence data were utilized for the years 1969–84, excluding 1972. There was no statewide cancer surveillance in 1972. Total and myelogenous leukemia rates are reported.

Age-adjusted, sex-specific incidence rates and 95 percent confidence intervals were calculated for each of the three groups using direct standardization as described by Fleiss.[6] The standard population utilized was the 1970 US population. Statistical testing for linear trend in incidence rates across the three groups was performed using a poisson trend statistic.[7]

Results

The age-adjusted incidence rates for total leukemia and acute granulocytic leukemia are shown in Tables 1 and 2. There was a weak positive relation between total leukemia rates and radioactivity in water, but a weak negative relation between acute granulocytic leukemia rates and radioactivity level consistent with either the hypothesis of no effect or of a small effect. As shown by the wide confidence intervals, the estimates of radioactivity-specific rates were rather unstable.

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TABLE 1—Age-adjusted Incidence of All Leukemias per/100,000 Person Years for 59 Iowa Towns (all ages), 1969–84

	Male		Female		Male & Female		Total Cases	
	Rate	(95% CI)	Rate	(95% CI)	Rate	(95% CI)	Male	Female
Group 1 (N=14)	17.2	(13.4, 21.0)	8.6	(6.3, 11.0)	12.0	(7.5, 16.5)	82	65
Group 2 (N=18)	16.3	(13.7, 18.8)	8.9	(7.2, 10.6)	11.8	(8.7, 14.9)	158	120
Group 3 (N=27)	16.1	(13.6, 18.7)	7.4	(5.8, 8.9)	10.9	(7.9, 13.9)	164	111

Group 1 = High, RA-226, > SPCi/L, 14 towns with an average population = 4,145 for a total of 812,616 person years.
Group 2 = Medium, 2.0 < RA-226 < 5.0 PCi/L, 18 towns with an average population = 8,155 for a total of 2,055,060 person years.
Group 3 = Low, RA-226 < 2.0 PCi/L, 27 towns with an average population = 4,154 for a total of 1,562,652 person years.

TABLE 2—Incidence of Acute Myeloid Leukemia per/100,000 Population for 59 Iowa Towns (all ages) 1969–84, excluding 1972

	Male		Female		Male & Female		Total Cases	
	Direct Rate	(95% CI)	Direct Rate	(95% CI)	Direct Rate	(95% CI)	Male	Female
Group 1 (N=14)	2.5	(1.1, 4.0)	1.2	(0.2, 2.1)	1.6	(0.5, 3.4)	12	8
Group 2 (N=18)	2.6	(1.6, 3.7)	1.3	(0.7, 2.0)	1.8	(0.6, 3.1)	24	17
Group 3 (N=27)	2.5	(1.5, 3.4)	1.8	(0.9, 2.6)	2.0	(0.7, 3.3)	25	22

Group 1 = High, RA-226, > SPCi/L, 14 towns with an average population = 4,145 for a total of 812,616 person years.
Group 2 = Medium, 2.0 < RA-226 < 5.0 PCi/L, 18 towns with an average population = 8,155 for a total of 2,055,060 person years.
Group 3 = Low, RA-226 < 2.0 PCi/L, 27 towns with an average population = 4,154 for a total of 1,562,652 person years.

Discussion

These data do not support the strong relation between radioactivity in drinking water and leukemia incidence suggested by the Florida study.

Published studies on the association of radium in water with cancer are aggregate studies and subject to the biases associated with such designs. The results of the Iowa and Florida studies may to some extent be explained by misclassification and confounding.

In the case of water studies, a more accurate measure of exposure would be based on the amount of radium^{-226} water consumed by each individual and the examination and adjustment for confounding etiologic factors. The amount of radium^{-226} in drinking water in these communities is subject to a variety of factors including home water softening, varying tap water consumption, duration of residence in the community, and so forth.

In the Florida study, a county was defined as high exposure on the basis of 10 percent of the sampled wells exceeding the EPA limit for radium. The Iowa study has the benefit of accurately defined exposure categories in a demographically stable area. Despite similar study designs, this study does not yield the strong association previously reported with leukemia. Future study of cancer incidence and radium concentration in drinking water in these and other communities is needed to clarify the risk of leukemia secondary to naturally occurring Ra^{-226}.

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Survey of Occupational Exposure of Waste Industry Workers to Infectious Waste in Washington State

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Abstract: We surveyed 940 Washington state waste industry workers to evaluate occupational exposure to potentially infectious materials (response rate 47 percent). Only 26 percent were trained specifically to deal with safety hazards associated with medical waste. For the year preceding the survey, 50 percent of respondents reported having received cuts and scratches on the job, 22 percent reported direct contact with waste blood on their clothing or shoes, 8 percent had blood exposure on their skin, 3 percent blood exposure on their face or eyes, and 6 percent occupational hypodermic needlestick injuries (10 percent among waste collectors). (*Am J Public Health* 1990; 80:1262–1264.)

Introduction

Medical waste disposal has recently emerged as a concern for waste industry workers. The AIDS (acquired immunodeficiency syndrome) epidemic has elevated waste worker concern regarding the potential for disease transmission from medical waste stream sources. Such transmission of AIDS or hepatitis B has never been epidemiologically demonstrated.[1]

Few studies have been conducted to examine waste industry worker exposure to potentially infectious agents in the waste stream. Gellin and Mitchell examined 97 waste workers employed by the City of Cincinnati during January and February of 1968 for skin disorders.[2] Forty-one cases of bacterial, viral, or fungal dermatitis were observed in this group, but all were classified as non-occupational in origin.

Cimino examined New York City Sanitation Department health records of waste workers employed between 1968–69.[3] Needlestick injuries were reported due to the presence of uncontained needles in waste collected from hospitals, physician's and dentist's offices, and discarded needles from drug addicts. All workers reporting needlestick injuries were given

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gamma globulin prophylaxis and no cases of hepatitis were reported.

A 1979 report by Clark, *et al*,[4] examined the incidence of viral infection among 43 waste collection workers. Sera antibody levels for 18 viruses were examined from blood samples collected during the spring and fall. The authors found no evidence of increased occupational risk to bloodborne viral infections.

This study was conducted to examine occupational exposure of Washington state waste industry workers to blood-contaminated waste and discarded hypodermic needles in the municipal waste stream.

Methods

The survey was conducted during February and March of 1989. Questionnaire packets were prepared and delivered to seven private sector waste industry firms and six public sector waste collection/disposal agencies. Selection focused on the state's population centers, although rural participation was included. Industry names were obtained through the Washington Utilities and Transportation Commission records and public sector solid waste utility listings. A total of 940 questionnaires were distributed to waste workers directly involved with waste collection or disposal within these firms or agencies. Based on the number of waste workers identified in the 1980 census which was adjusted for population growth and a review of non-participating firms, the surveyed workers account for approximately 70 percent of the waste industry workforce in Washington state.

Participant responses were confidential and not individually identified. Questionnaires were returned directly to the research group by the participants in stamped return envelopes without review by their respective waste industry employers.

Participants included those involved with residential waste collection, commercial collection, and landfill/transfer station operations. Waste worker job categories included heavy equipment operators, truck drivers, collectors, equipment maintenance personnel, laborers, recyclers/sorters, gatekeepers/scalehouse operators, and field supervisors.

Survey variables included the respondent's job category, job safety training, occupational observance of medical waste, exposure to blood-contaminated waste, and occurrence of hypodermic needlestick injuries. Questions regarding occupational exposures or injuries requested that the respondent include the month and year of his/her most recent event to discourage a positive response unless a specific occurrence could be recalled.

Results

Of 940 surveys distributed to waste workers, 438 were returned (47 percent). Of these, 52 percent of respondents conducted all or part of their job activities in residential waste collection, 41 percent in commercial waste collection, and 38 percent in landfill/transfer station operations.

Sixty-nine percent of the respondents reported receiving job safety training. Twenty-six percent indicated that this training included medical waste safety practices. Ninety percent of the respondents reported observing medical waste (e.g. needles, blood, bandages) in the waste stream. Of this group, the frequency of observation of medical waste was identified as daily by 27 percent of this group, weekly by 40 percent, monthly by 17 percent, yearly by 8 percent and less than once a year by 8 percent.

Injury/exposure information for occupational cuts and scratches, blood exposures, and needlestick injuries is based on the respondent's recall for events occurring on at least one occasion. Such information reported for the year preceding the survey required the respondent to include both the month and year of their most recent event.

Cuts and scratches received on the job were reported by 74 percent of the respondents. For the year preceding the survey, such injuries were reported by 50 percent of respondents.

Thirty-two percent of the respondents reported having experienced direct contact with blood on their clothing or shoes, 13 percent on their skin, and 5 percent on their face or eyes. For the year preceding the survey, 22 percent reported having experienced direct contact with waste blood on their clothing or shoes, 8 percent had blood exposure on their skin, and 3 percent had blood exposure on their face or eyes.

Twenty-one percent of responding waste workers reported having been stuck or scratched by a waste hypodermic needle. Six percent reported that their most recent injury occurred within the year preceding the survey. Such injuries were reported by 10 percent of waste collectors within the same time period. Needlestick injuries were reported by 24 percent of respondents for residential waste collection, 21 percent for commercial waste collection, and 11 percent for landfill/transfer station operations. Needlestick events by individual job category are presented in Table 1.

Discussion

In this survey, the low response rate (47 percent) may have resulted in a higher estimated incidence of exposure; exposed individuals should be more likely to respond if an exposure is a memorable experience. If one assumes that none of the non-responders had experienced an exposure and only respondents who could give both the month and year of the event actually experienced an exposure, the estimated exposure incidence among the 940 persons sent a questionnaire for the year preceding the survey would be 10 percent (blood exposure to clothing or shoes), 4 percent (blood exposure to skin), 1.5 percent (blood exposure to face or eyes), and 3 percent (needlestick injuries).

Of greatest potential significance to waste worker health was the reporting of needlestick injuries. Written survey comments from workers described loose needles originating from uncontained disposal or ruptured sharp containers in the waste stream. Needles were identified originating from both residential and medical facility sources. Accounts of uncontained

TABLE 1—Needlestick Injury by Waste Worker Job Category for the Year Preceding the Survey

Primary Job Category	Number (%) of Respondents	Number and Proportion (%) of Respondents Reporting Needlestick Injury
Heavy Equipment Operator	27 (6)	1 (4)
Truck Driver	79 (18)	2 (3)
Collector	241 (55)	23 (10)
Equipment Maintenance	19 (4)	1 (5)
Laborer	23 (5)	1 (4)
Recycler/Sorter	2 (0.5)	0 (0)
Gatekeeper	23 (5)	0 (0)
Field Supervisor	18 (4)	0 (0)
Total	432	28 (6)

*Needlestick response requires respondent noting month and year of occurrence.

needles and the reporting of needlestick injuries sustained by waste workers indicate the need for proper handling, containment and/or destruction of needles by users prior to disposal.

Observation of medical waste (e.g. needles, blood, bandages) in the general waste stream was common (90 percent of respondents). Further study to identify frequency of occupational exposure to blood is recommended, especially in relation to proposed standards for bloodborne pathogens by the US Department of Labor, Occupational Safety and Health Administration.[5]

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Fear of AIDS and Attrition among Medical Technologists

RONALD R. GAUCH, PHD, KAREN B. FEENEY, MPA, AND JAMES W. BROWN, PHD

Abstract: Attitudes toward AIDS were measured by a survey of 212 attendees at the annual meeting of the New Jersey Society for Medical Technology. Twenty five percent of the respondents were considering leaving the profession because of a fear of AIDS. In addition, almost half would not have chosen the field knowing they would be handling HIV-positive samples. This high degree of concern may be an important factor contributing to the shortage of medical technologists. (*Am J Public Health* 1990; 80:1264–1265.)

Introduction

A 1988 survey by the American Society of Clinical Pathologists reported that 9 percent of medical technologists positions are vacant and more than 75 percent of laboratory managers perceive a shortage of qualified laboratory personnel.[1] The shortage among medical technologists has been attributed to a wide spectrum of problems: low pay with a compressed salary structure, lack of upward mobility, job stress, poor working conditions, lack of professional recognition, and increased opportunities in other professions that have commensurate educational requirements.[2,3]

A survey conducted in 1987 among New England laboratories, reported that 39 percent of the respondents mentioned fear of AIDS (acquired immunodeficiency syndrome) as a reason laboratory workers leave the profession.[4] A 1987 study, confined to medical technologists, also found a high fear of acquiring AIDS.[5] The purpose of our study was to describe attitudes of medical technologists toward working with AIDS-infected samples.

Methods

A questionnaire was designed which included 15 questions using Likert rating scales with the response options ranging from strongly agree to strongly disagree. Independent variables included demographic and institutional factors. Three additional questions dealt with an individual's knowledge of AIDS.

The questionnaire was distributed to registrants at the 1988 annual meeting of the New Jersey Society for Medical Technology. Of the 295 registrants, 283 were given forms to be filled out anonymously and 212 were returned (75 percent).

Results

The results showed that fear of AIDS among laboratory workers is common (Table 1). For example, 52 percent agreed with the statement that, despite precautions, it was likely that they could become infected with HIV because of laboratory exposure and 41 percent would like to transfer to a position that required less blood handling. Only 43 percent indicated that they would have chosen the profession knowing they would be handling samples from AIDS patients and one out of four respondents is considering leaving the profession because of a fear of AIDS.

Medical technologists are clearly experiencing pressure to seek a different career. In 86 percent of those queried, respondents reported that friends and family members expressed concern about their working with HIV samples and 53 percent knew of colleagues who had left the profession because of the possibility that they could acquire the human immunodeficiency virus (HIV).

On the other hand, there was general satisfaction with employer safety policies. Three out of four felt their employer provided adequate education concerning HIV risk and that adequate safety measures, which lower the risk of HIV transmission, were available. However, less than half felt that their employer offered adequate counseling in the event of an accident.

It was apparent that the AIDS problem had resulted in improved safety practices within the profession. For example, increased reporting of needlestick injuries and the wearing of gloves were reported by 87 percent and 94 percent of the respondents, respectively.

Not surprisingly, those currently working were more inclined to contemplate a career change than people about to enter the field. One in three of employed medical technologists was thinking about departing the profession because of their fear of AIDS. In contrast, only 13 percent of the students surveyed indicated they were planning to take such a step.

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TABLE 1—Percent of Respondents in Agreement with Survey Questions

Questions	Percent Agreement*
Fear of Acquiring AIDS Questions	
I feel I have the right to be informed of HIV + samples.	96
I believe that fear of acquiring HIV is a major reason for the low enrollments in the MLT and MT schools.	77
Despite precautions, I believe it is likely I could become infected with HIV because of laboratory exposure.	52
In retrospect, I would have chosen the field of medical technology knowing that I would be handling samples from AIDS patients.	43
I would like to remain in the field but would like to transfer to a position that requires less blood handling because of my fear of acquiring AIDS.	41
I am considering leaving the profession because of my fear (and/or my "significant other's" fear) of acquiring HIV in the laboratory.	25
Pressure to Leave the Profession Questions	
I have had friends or family express concern about my working with HIV positive samples.	86
I know of colleagues who have left the clinical laboratory profession because of their fear (and/or their "significant other's" fear) of acquiring HIV in the laboratory.	53
Employer Safety Policies Questions	
I feel that infection control practices in my lab have improved because of fear of acquiring HIV.	79
I feel my employer provides adequate education on HIV risk.	77
I feel my employer has provided adequate safety measures that lower the risk of HIV transmission in the laboratory.	75
I feel my employer offers adequate counseling in the event of an accident with HIV positive samples.	41
Employee Safety Practices Questions	
Because of the risk of contracting AIDS I am more likely to wear gloves today than in the past.	94
Because of the risk of contracting AIDS, I am more likely to report needlestick injuries than in the past.	87
I feel that universal blood precautions will change the way I currently handle samples.	72

*Percent based on a response of strongly agree or agree.

Further analysis was carried out on the group working in the field to determine if there were any important differences between those considering and those not planning a career change. No important differences were present in respect to age, sex, salary level, marital status, responsibility for dependent children, education level, or working environment (hospital or nonhospital work). Furthermore, the two groups were similar in respect to their knowledge of AIDS (i.e. awareness of the transmission, etiology, and diagnosis of AIDS). The only demographic variable that distinguished the two groups was position in the organization. Of those with supervisory responsibilities, 18 percent were considering a job change versus 38 percent of those without supervisory responsibilities (data available upon request to authors).

Discussion

These findings suggest that fear of acquiring AIDS contributes to the attrition rate among medical technologists. On a positive note, it was found that medical technologists tend to be satisfied with employer AIDS policies. There was, nevertheless, concern on the part of a majority of workers about the lack of a counseling program in the event of a laboratory accident. Employers can help reduce this anxiety by having counseling programs in place and making sure workers know they exist.

The survey found that because of AIDS, glove use increased substantially. However, when asked how often they wear gloves, only 46 percent responded that they wore gloves all the time. It therefore appears that laboratory management needs to be more active in motivating their staffs to wear gloves on a regular basis. The Occupational Safety and Health Administration's mandate for routine glove use, which came out after the survey was completed, places an even greater responsibility on the part of management to see to it that employees use safe practices.

It is also important to note that universal blood precautions, where all samples are to be considered infectious, were in effect when the survey was taken. Still, the overwhelming majority of the respondents (96 percent) felt they had the right to be informed of HIV positive samples. This situation illustrates a common dilemma facing the health care community—a patient's right to privacy and an employee's "right to know."

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Are Women Using Postmenopausal Estrogens? A Community Survey

ROBIN B. HARRIS, PHD, AMI LAWS, MD, VENUGOPAL M. REDDY, MBBS, ABBY KING, PHD,
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Abstract: Self-reported estrogen and progestin use in a California community was determined in 1986–87 from a telephone survey of postmenopausal women ($n = 954$) ages 50–65 years. Current use of hormones was reported by 32 percent; 26 percent took estrogens alone while 6 percent used estrogen + progestin. Comparisons pointed to significant social network and medical care utilization differences. Women who used estrogen therapy were younger, thinner, lived in smaller household units, and were less likely to be widowed. (*Am J Public Health* 1990; 80:1266–1268.)

Introduction

Postmenopausal estrogen use has fluctuated in the past three decades, based on changing perceptions of its associated risks and benefits.[1-11] Currently, estrogens are advocated[12] because of their beneficial effect on serum lipids[13-16] and their protective effect against osteoporosis[10,11] and cardiovascular disease,[17-22] although the risk of cancer with prolonged use remains a concern.[3,8,9,23] Several studies have examined the effect of these changing perceptions on clinical practice.[24-26] Physicians in the mid-1980s report prescribing postmenopausal estrogen to far more of their patients than in the 1970s, although they are prescribing lower doses with an added progestin.[25,26]

We report postmenopausal hormone use in a defined community in 1986.

Methods

Between October 1986–April 1987, a random-digit dial telephone survey was completed of persons ages 50–65 years residing in Sunnyvale, California, a relatively affluent community located at the southern end of the San Francisco peninsula. Only one individual per household was interviewed, with decisions as to whom to interview made using a random allocation procedure. At least five calls were attempted to the household. The phone company estimates that over 97 percent of the households have telephones. The response rate among age-eligible women was over 72 percent.

Postmenopausal women were asked whether they were currently using any prescribed medications and to name the specific medications and dose by reading from the prescription labels. Hormone use was classified by major type of therapy: use of estrogens alone versus use of estrogens plus a progestin. Other questions, adapted from the 1985 National Health Interview Survey,[27] determined social and demographic characteristics, use of other medications and alcohol, exercise and smoking behavior, a brief medical history, and perceptions of current health status. Body mass index (kg/m^2) was calculated from self-reported height and weight.

This report is based on 954 postmenopausal women between ages 50–65 years. Only 45 women were excluded because of missing information on menopausal status or medication use.

Bivariate contingency tables were constructed to assess association between use of estrogens and the interview questions. Multivariate analyses used the logistic model to assess independence of the variables. Adjusted odds ratios and their 95% confidence intervals for estrogen use were calculated from the logistic coefficients and their standard errors[28] and to test for statistical significance of age interaction terms.[29] The dependent variable was coded as use or nonuse of estrogen hormones. Age and body mass index were modeled as continuous variables. Number of members in the household was an ordinal variable coded 0–6+; other independent variables were coded as presence or absence of the history or event.

Results

In this population, 32.2 percent ($n = 307$) of the women reported current use of postmenopausal estrogens. Of the 307 users, 18 percent (5.9 percent of the total population) reported also taking a progestin. Use was highest in the younger women, with 40.6 percent of women ages 50–54 reporting use compared to 23.1 percent of women ages 60–65 years. The use of progestins also decreased with age, from 9.4 percent of women ages 50–54 years to 2.8 percent of women 60–65 years.

Eighty-three percent of the hormone users identified a specific medication, or a dose if the estrogen was a generic conjugated estrogen. Premarin was the predominately named estrogen (65 percent), followed by the generic conjugated equine estrogens (27 percent). Forty percent of conjugated estrogen users named the .625 mg dosage. Provera accounted for 63 percent of progestin use, with 46 percent of these users naming the 10 mg dose.

Self-reported demographic and health behavior characteristics are shown in Table 1. Users were thinner, reported more regular aerobic exercise, had fewer people living in their households, and were less likely to be a widow than were the nonusers.

There were no differences between users and nonusers in their history of high cholesterol, diabetes, or heart problems (Table 2). Users were less likely to have a history of high blood pressure or stroke, but more frequently reported being under the care of a physician for other medical conditions.

Table 3 shows the results of the multivariate analyses. Age of the woman, body mass index, number of individuals in the household, and widowhood remained independent correlates of postmenopausal hormone use. Other logistic regression models showed history of high blood pressure, aerobic exercise, and presence of other medical conditions were not independently related to the hormone use. In addition, no significant age interactions were demonstrated. Similar analyses were performed to compare estrogen-only use with estrogen + progestin use; age was the only variable independently related to estrogen + progestin use.

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TABLE 1—Descriptive Information on Sociodemographic and Health Behavior Variables for Users and Nonusers of Postmenopausal Hormones in the Sunnyvale Population, 1986

Characteristics	Postmenopausal Hormone Users n = 307*	 Nonusers n = 647*
Marital status		
% Married	59.6	59.8
% Widowed	9.1	14.9
% Currently employed	61.2 (304)	58.6 (642)
Education, mean ±sd	13.7 ± 2.6	13.6 ± 2.8
Ethnicity: % White	91.9	88.4
Household size, mean number ± sd	2.0 ± 0.8 (295)	2.4 ± 1.2 (628)
% Current smoker	24.6	26.7
% Aerobic exercisers	23.5 (302)	17.5 (642)
Body Mass Index, mean kg/m² ± sd	24.0 ± 3.9 (306)	25.4 ± 4.9 (631)
Alcohol use, mean drinks/2 weeks ± sd	10.4 ± 14.1 (240)	8.5 ± 10.9 (428)

*Total number of users and nonusers, if number different then given in parentheses.

TABLE 2—Self-reported Medical Conditions of Users and Nonusers of Postmenopausal Hormones

	Postmenopausal Hormone			
	Users		Nonusers	
Characteristics	%	N	%	N
History of high blood pressure	28.0	(304)	37.2	(645)
History of stroke	00.3	(307)	3.1	(646)
History of high cholesterol	21.8	(294)	20.6	(622)
History of diabetes	3.2	(285)	5.5	(599)
History of heart problems	6.2	(307)	6.2	(638)
Other medical conditions	23.7	(304)	18.1	(643)
Hospitalizations in past year, mean ± sd	0.2 ± 0.5	(298)	0.2 ± 0.6	(630)
Perceived health rating* mean ± sd	1.8 ± 0.7	(307)	1.9 ± 0.8	(646)

*Health rated as Excellent (1), Good (2), Fair (3), Poor (4).

TABLE 3—Adjusted Relative Odds for Postmenopausal Estrogen Use by Behavioral, Sociodemographic and Reported Medical Conditions

Characteristic	Adjusted* Odds Ratio	(95% CI)
Age trend per year	.92	(.89, .95)
Body mass index trend (kg/m²)	.93	(.90, .97)
Household size trend (no./household)	.66	(.55, .78)
Widowed	.49	(.30, .82)

*Adjusted using a logistic regression model that included the variables listed on this table, n = 294 users and 612 nonusers.

Discussion

This 1986 community survey shows self-reported current use of PMH (32 percent) is less than expected when compared to recent physician surveys indicating 75–95 percent of gynecologists would prescribe estrogen therapy to most of their patients[25,26] and to estimates from pharmaceutical marketing surveys of 43 percent use among women living in the western part of the United States.[7] The use rate is similar to a recent report from another California community.[30] The use of progestin combined with the estrogen is also less than expected and less than previously reported,[30] with 18 percent of the users reporting a progestin component.

While response bias, i.e., women not knowing or remembering what medications they are currently taking, could have contributed to the low postmenopausal hormone use, it is unlikely to be the major explanation of these discrepancies. Over 80 percent of the estrogen users were able to name their specific medication and dose. Since hysterectomy status was not ascertained in this survey, it is impossible to know what percent of women with an intact uterus were using unopposed estrogens. However, this limitation would not have contributed to an underestimate of total use. A high hysterectomy rate in Sunnyvale could explain the lower use of progestins than seen in the Rancho Bernardo study.[30]

The taking of PMH by women is the outcome of several factors, notably: local physician prescribing practices, medical care utilization patterns, drug side-effects, and social network or information sources of the women. Differences between women who use and do not use estrogens can, therefore, be due to underlying social or behavioral differences as well as to actual drug effects.

As in other surveys,[31,32] the youngest women, who were most likely to be recently menopausal, had the highest current estrogen and progestin use. This pattern probably reflects the effort to control menopausal symptoms as well as to decrease bone density loss. Younger women reached menopause at a time physicians were increasing their postmenopausal hormone prescribing.

The findings of thinner women more likely to use hormones was also shown in the earlier surveys.[31,32] This difference may reflect increased menopausal symptoms in thinner women due to their decreased endogenous estrogen levels, or more prescribing by physicians because of increased risk of osteoporosis in thinner women.

Women who were widowed were less likely to be on estrogen therapy than women who were currently married, but women who used hormones had fewer people living in their households. These findings may reflect basic social network differences between users and nonusers: e.g. nonusers may be major caretakers of other family members and less likely to have the time or inclination to care for themselves; a recent study of persons over age 65 reported that people who live with others go to doctors less often.[33]

In summary, this survey shows a discrepancy between published physician enthusiasm for PMH and low reported use by women. Comparisons between users and nonusers reflect differences in physician prescribing patterns, social networks, and health care utilization patterns.

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Estimating the Mortality Cost of AIDS: Do Estimates of Earnings Differ?

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Abstract: The future earnings of male Texans dying of AIDS in 1987 were estimated using: national earnings profiles; earnings derived from occupations listed on death certificates; and earnings reported by persons with AIDS who responded to a survey. Mortality cost estimates using the two sources of actual earnings differed by a modest amount in comparison to the estimate using national earnings profiles. (*Am J Public Health* 1990; 80:1268–1270.)

Introduction

Because of the relative youthfulness of persons with acquired immunodeficiency syndrome (AIDS), the cost to society from the loss of earnings of those who die prematurely is an important concern in measuring the impact of the disease. Two published studies have attempted to determine this cost using the foregone earnings approach. Hardy and coworkers estimated the present value of the foregone earnings of the first 10,000 AIDS cases at $4.6 billion, over three times their estimate of total hospital expenditures (approximately $1.4 billion) for these cases.[1] Scitovsky and Rice estimated the current value of foregone earnings associated with AIDS deaths in 1986 at $6 billion, approximately six times their estimate of personal medical care costs ($1.0 billion).[2]

These estimates may be criticized because of the absence of actual earnings data in estimating the present value of future earnings lost. The foregone earnings method uses national cross-sectional profiles of earnings and labor force participation rates by age and sex.[3] It is simply assumed that a person with AIDS has the same employment and earnings pattern as other Americans in his or her age and sex cohort.

This paper examines this assumption by comparing estimates of the foregone earnings of males who died of AIDS in Texas in 1987 using national earnings profiles and two sources of actual earnings.

Methods

To derive the first estimate, we followed the standard practice of multiplying the present values of lifetime earnings

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by age category, derived from national earnings profiles, by the corresponding number of AIDS deaths in Texas and summing the products across categories. The present value of future earnings by age, reported by Scitovsky and Rice for 1984,[2] were updated using the ratio of mean earnings for full-time workers in 1987[4] as compared to those in 1984.[5] The age characteristics of males who died of AIDS in 1987 were supplied by the Texas Department of Health.

The occupational status (obtained from death certificates) of a 10 percent random sample (N = 96) of males who died of AIDS in 1987 was the basis for the second estimate of mortality costs. The occupations of these persons were translated into average annual earnings using occupation-specific wage data for the Houston and Dallas-Ft. Worth SMSAs from the Bureau of Labor Statistics, US Department of Labor.[6,7]

The third estimate used earnings derived from a statewide survey of living persons with AIDS.* In the summer of 1988, a convenience sample of 1,083 persons with human immunodeficient virus (HIV) infection being served by community-based AIDS service organizations, physicians' offices, and other service providers were asked to complete an anonymous, self-administered questionnaire. The questionnaire requested information on occupation and income at the time of first HIV-related diagnosis. Forty percent (434) of the questionnaires were returned; 280 respondents (six females, 274 males) had an AIDS diagnosis. These individuals represented about 15 percent of all AIDS cases estimated to be alive in Texas at the time of the survey. Of the male respondents with AIDS, 228 (83 percent) supplied income information. Since the survey excluded persons outside the larger metropolitan areas of the state, illiterate and/or poorly educated individuals, and Spanish-speaking persons, it does not represent the state as a whole.

Mean earnings for males with AIDS in different age groups was derived, based on each source of actual earnings. Comparisons were made with national mean earnings reported by the Bureau of Census.[4] Percentage differences for each group were calculated and used to adjust the present value of expected lifetime earnings for the corresponding group. The adjusted earnings figures were then multiplied by the number of AIDS deaths in Texas in 1987 by age category and summed across categories to obtain mortality cost estimates. The cost estimate effect of each data source was subjected to sensitivity analysis to allow for errors in the estimates of actual earnings.

Results

Although obtained in different ways, the survey and death certificate samples were not significantly different from the Texas AIDS case registry with respect to age (Table 1). However, Blacks were underrepresented in the survey sample and Whites were overrepresented. There were more individuals with low wage occupations in the survey than in the death certificate sample.

The average annual earnings of male persons with AIDS in Texas, based on the death certificate sample, was 11 percent below the national average (Table 2). However, it was .3 percent above the national average when based on the survey sample.

TABLE 1—Comparison of Age, and Occupational Characteristics: Survey Sample, Death Certificate Sample, and Case Registry

	Information Source		
Characteristics	Survey (N = 228) %	Death Certificates (N = 96) %	Texas AIDS Case Registry, 9/2/88 (N = 4926) %
Age (years)			
20–29	20.7	24.7	25.9
30–39	53.3	51.5	48.2
40–49	21.6	18.6	17.7
50+	4.3	6.2	7.8
Ethnicity			
Black	2.2	No Data	11.6
White	86.7		77.0
Hispanic	8.8		11.1
Other	1.8		0.3
General Occupation			
Professional/Technical	37.4	43.3	No Data
Clerical/Sales	23.3	19.6	
Service	27.8	16.5	
Other	11.5	20.6	
Agriculture/Fishing	0.9	1.0	
Processing	0.4	—	
Machine Trades	1.8	—	
Benchwork	1.8	4.1	
Structural	4.8	13.4	
Miscellaneous	1.8	2.1	

TABLE 2—Comparison of Current Earnings: National Profiles, Survey Sample, and Death Certificate Sample[a]

National[b]		Survey			Death Certificate		
Age Group	$	#	$	%Diff.	#	$	%Diff.
20–24[c]	9,009	5	11,100	23.2	5	18,252	103.0
25–29	19,570	43	15,692	−19.8	18	18,694	−4.5
30–34	24,485	70	23,840	−2.6	33	22,393	−8.5
35–39	29,019	52	28,574	−1.5	17	20,891	−28.0
40–44	32,314	31	29,107	−9.9	9	27,716	−14.2
45–49	33,655	18	25,388	−24.6	8	23,289	−30.8
50–54	32,581	6	28,600	−12.2			
55–59	28,422	2	33,250	17.0	4	25,207	−11.3
60–64	26,800	1	20,000	−25.3			
>64	15,460				2	0	−100.0
Total	24,015	228	24,098	0.3	96	21,442	−10.7

[a] Foregone earnings based on national, survey, and death certificate estimates of current earnings: $743.4 million, $697.2 million, $656.4 million. Ten percent variations in the current earnings estimates produced foregone earnings ranging from $627.5 million to $772.4 million.

[b] Source: Reference 4.

[c] The national data include ages 18–24.

The present value of lifetime earnings lost for male AIDS deaths in 1987 was $743 million based on national earnings profiles, $697 million based on earnings from the survey, and $656 million based on earnings derived from the death certificate sample. The two estimates using actual earnings were below the national earnings estimate by 6 percent and 12 percent, respectively. Given the possibility of error in the sample estimates of actual earnings, mortality costs were recalculated using earnings of 10 percent above and below the sample estimates for each age group. These variations lead to differences in mortality cost estimates ranging from 4 percent above to 15 percent below the national estimate.

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*Crane, MM, Jardine L, Tortolero S, Hines A, Johnson C: Survey of Texans with HIV infection: medical, social service and financial needs. Unpublished report for the Texas Legislative Task Force on AIDS. December 21, 1988.

Discussion

The mean earnings of male Texans with AIDS, based on occupational status, was found to be 12 percent below the national average. However, self-reported earnings from a sample survey averaged less than 1 percent above the national average. It is possible that bias in the survey sample could account for the difference. As noted earlier, it is likely that the survey sampling procedure reduced participation by individuals at the lower end of the income spectrum.

The effect of using the two sources of actual earnings rather than national earnings to estimate future earnings lost was a relatively small reduction. The differences remained relatively small after increasing and decreasing actual earnings estimates by 10 percent. This finding suggests that the additional effort required to obtain actual earnings for persons with AIDS in order to calculate the foregone earnings of premature mortality was not necessary in this case. However, further studies are needed to determine if the findings hold in less biased samples in other areas of the country and for the changing AIDS population.

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Sociodemographic Correlates of Neutralizing Poliovirus and Hepatitis A Virus Antibodies as Markers of Different Modes of Acquiring Immunity

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Abstract: The prevalence and sociodemographic correlates of antibodies against poliovirus and hepatitis A virus (HAV) were compared in a random sample of 457 military recruits in Israel inducted during 1987. Lower socioeconomic status (SES) was associated with a higher prevalence of anti-HAV antibodies (67.3 vs 32.5 percent), whereas the reverse was true for type 1 poliovirus (78.4 vs 89.5 percent). While the high prevalence of anti-HAV antibodies observed in the lower SES groups reflects considerable natural exposure to enteroviruses, immunity against poliovirus appears to be determined primarily by compliance with vaccination. (*Am J Public Health* 1990; 80:1270–1271.)

Introduction

Between 1961–83, the annual incidence of poliomyelitis in Israel ranged from three to 35 cases.* It was felt that the population should have high levels of immunity through vaccination, but enhanced immunity acquired through continuous exposure to wild virus in the environment was also considered possible. Both the hepatitis A virus (HAV) and the poliovirus are transmitted by the fecal-oral route. Ethnic and educational differences in HAV infection have been demonstrated in Israel[1,2] and elsewhere.[3] We compared the sociodemographic correlates of antibodies against both HAV infection and poliomyelitis as markers of the modes of acquiring immunity to these diseases.

Methods

Sera stored at −20°C which had been taken from a random sample of 494 military conscripts in Israel in 1987 were used for the serological studies.

Sociodemographic data included age, country of origin, education and socioeconomic status (SES). Country of origin was defined by the father's birthplace (or where this was Israel, the paternal grandfather's birthplace). Those from Europe (excluding Turkey), the Americas, Australasia and Southern Africa were defined as Westerners. All other birthplaces, except Israel, were classified as Easterners. To simplify the classification, those whose father and paternal grandfather were born in Israel were excluded from the analyses, leaving a sample size of 457.

The normal approximation was used to compute 95 percent confidence intervals for difference between percentages. Multiple logistic regression analysis was used to determine correlates of antibodies while controlling for other potentially confounding factors.

Hepatitis Serology

The anti-HAV antibody studies were performed at the central Israel Defense Force laboratories by means of solid

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*Israel Ministry of Health, publications on selected infectious diseases 1961–88.

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phase radioimmunoassay (HAVAB-Abbott Laboratories, N. Chicago, IL).

Polio Serology

The neutralizing poliovirus antibody studies were carried out at the Israeli Central Virology Laboratory. The sera were inactivated before testing in a microneutralization system. Serial four-fold dilutions were prepared in microtiter plates and between 30 and 100 TCD_{50} of wild poliovirus (Mahoney--type 1, MEF—type 2, Saukett—type 3) were added. The mixtures were incubated at 36°C for 20 hours, followed by the addition of Hep-2 cells. Following incubation, fixation, and staining, the plates were examined macroscopically and titers were defined as the highest dilution of serum that completely inhibited cytopathic effect. In this study, antibody titers greater than 1:4 were regarded as positive. Since large inter-laboratory differences have been demonstrated,[4] caution should be exercised in comparing these titers with those obtained in other laboratories.

Results

The prevalence of anti-HAV antibodies was substantially lower for Westerners (30.9 percent of 201) than for Easterners (57.0 percent of 256) (95% CI for the difference was 17.0, 35.4). The prevalence of neutralizing poliovirus antibodies was slightly lower for Easterners for all three types: type 1—82.0 percent vs 89.6 percent, type 2—98.1 percent vs 98.5 percent, type 3—83.2 percent vs 86.6 percent. The prevalence of anti-HAV antibodies was substantially higher for subjects of lower SES (67.3 percent of 171 vs 32.5 percent of 286; 95% CI for the difference 25.3, 44.2) whereas the prevalence of neutralizing poliovirus antibodies was greater for higher SES (89.5 percent of 286 versus 78.4 percent of 171; 95% CI for the difference 4.1, 17.5). In multiple logistic regression analysis (Table 1), low SES and Eastern origin were positively associated with the presence of anti-HAV antibodies after adjusting for education and sex. For type 1 poliovirus, high SES was positively associated with higher antibody titers after adjusting for the other variables.

TABLE 1—Multiple Logistic Regression Adjusted Odds Ratios (with 95% confidence intervals) for the Association between the Presence of Anti-Hepatitis A Antibodies and Neutralizing Poliovirus Type 1 Antibody Titers >1:4 with Sociodemographic Variables in 18–19 year-old Jews in Israel Examined in 1987

	Anti-HAV Antibodies	Poliovirus type 1 antibodies
Variable	Odds ratio (95% CI)	Odds ratio (95% CI)
Sex (Male = 0)	1.22 (0.81–1.83)	1.22 (0.71–2.10)
Ethnic origin (West = 0)	2.29 (1.52–3.46)	0.63 (0.35–1.12)
Years of education (<12 yr = 0)	0.83 (0.46–1.50)	1.42 (0.70–2.89)
Socioeconomic status (High = 0)	3.75 (2.31–6.09)	0.40 (0.22–0.74)

CI = Confidence interval

Discussion

The higher prevalence of anti-HAV antibodies in 18–19 year old Jews of Eastern origin compared with those of Western origin, found in earlier studies,[1] has persisted. The prevalence was also found to be independently higher in those of lower SES. This indicates continuing differential exposure of subpopulations in Israel to viruses transmitted by the fecal-oral route, possibly due to spread among children particularly in large families.[2,5]

The associations of SES and ethnic origin with neutralizing poliovirus antibodies were opposite to those found for HAV. This finding would tend to exclude any significant natural exposure to wild poliovirus. The lower prevalence of immunity against polio among those of Eastern origin and lower SES may be due to variation in immunization coverage in different segments of the population[6] or differences in the uptake of oral poliovaccine due to interference by concurrent gastrointestinal infections.

The findings in the present study suggest that subgroups in this population who are more susceptible to HAV infection are less likely to have high levels of neutralizing poliovirus antibody titers. Thus while HAV appears to be widely transmitted under lower socioeconomic conditions, immunity against poliovirus in Israel over the past 20 years appears to have been determined primarily by compliance with vaccination. If the new HAV vaccine currently being tested becomes routine in childhood, immunity will be determined mainly by vaccine compliance.

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